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The American Heart Journal

CONTENTS FOR OCTOBER, 1930

Symposium on Cardiovascular Syphilis

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Symposium on Cardiovascular Syphilis

The papers which follow constitute the program of the meeting of the American Heart Association held in Detroit on June 24, 1930, and represent the first fruits of the efforts of the Committee for the Coordination of Investigation of that Association to encourage coordinated research in the various phases of cardiovascular disease.

SYPHILIS OF THE AORTA AND HEART*

HARRISON S. MARTLAND, M.D.
NEWARK, N. J.

PART I

ANATOMICAL TYPES ENCOUNTERED BY THE WRITER, AS MEDICAL EXAMINER IN CASES OF SUDDEN DEATH

UNTIL approximately ten years ago acquired syphilis as it affected the heart was thought to be chiefly a disease of the aorta and aortic valve producing aortic regurgitation, aneurysm or narrowing of the orifices of the coronary arteries.

Warthin is responsible for what is called the newer pathology of cardiac syphilis.

Warthin[1] in 1911 in a study of twelve cases of congenital syphilis affecting the heart, chiefly in infancy and childhood, concluded that the characteristic lesion is a diffuse or localized interstitial myocarditis in which *Spirochaeta pallida* can be demonstrated. In later life this may lead to the fibrous heart.

In 1914 after a study of 200 hearts in which spirochetes were found, he[2] stated that many cases of cardiac syphilis were not being recognized.

In 1918 he[3] reported an incidence of 40 to 50 per cent of syphilis in his necropsy service, as compared to 6.5 per cent found by Symmers. He stated that the gumma was no longer the criterion for the diagnosis of syphilis but that milder, more diffuse, specific inflammatory processes occurred which eventually lead to fibrosis. Based upon the demonstration of spirochetes in various organs he estimated that about 30 per cent of the population was syphilitic.

*From the Pathological Department of the City Hospital, Newark, N. J., and the office of the Chief Medical Examiner of Essex County, N. J.

In 1925, based upon the study of eight hearts from cases of sudden death, collected over a period of twenty years, he[4] attributes sudden death to an acute exacerbation of previously mild latent processes in the heart and aorta. The chief gross lesions were "patchy areas and streaked areas of pale, yellowish, grayish-yellow or gray color, without hemorrhage or congestion, scattered throughout the myocardium." He believes that such areas may easily be mistaken for anemic infarcts. Microscopic examination shows areas of old fibrosis (healed myocarditis), subacute infiltrations of lymphocytes and plasma cells between the muscle fibers, with angioblastic and fibroblastic proliferation and interstitial edema; more acute areas of interstitial edema with infiltration of lymphocytes, plasma cells, monocytes and a predominance of polymorphonuclears. Spirochetes were found, particularly in these more acute areas.

Clawson and Bell,[5] in a study of 126 hearts associated with syphilitic aortitis collected over a period of sixteen years in an attempt to observe the anatomical changes in the valve, coronary arteries, myocardium and pericardium and to note the immediate relation of these changes to the cause of death, carefully followed Warthin's technic for the demonstration of these myocardial lesions.

In twenty-eight hearts showing aortic insufficiency they concluded that the main myocardial lesion was hypertrophy, and that little significance could be attached to any other gross or microscopic changes in the myocardium. Most of the small fibrotic areas were evidently a result of slight nonsyphilitic coronary injury, and were not of sufficient degree to be a factor in heart failure. Syphilis of the myocardium in these twenty-eight hearts was apparently rare, and when present was of insignificant degree. "With the exception of the hypertrophy, we found no anatomic change in the myocardium which seems sufficient to cause death." Spirochetes could not be found in any of the twenty-eight hearts.

In fifteen hearts from cases of sudden death attributed to closure of the coronary orifices, gross myocardial fibrosis was not observed, nor were infarcts, commonly found in cases of senile coronary sclerosis, present. Microscopic myocardial fibrosis was seen only in four cases. Its infrequency and the slight degree when present led them to think that it had little or nothing to do with cardiac failure in these hearts. Thirteen of these hearts were stained for spirochetes and none were found.

In twenty-three hearts with ruptured aortic aneurysms gross myocardial fibrosis was not present. Microscopic fibrosis to a slight degree was found about the aortic ring in four cases. No spirochetes were found in any of the cases.

The work of Clawson and Bell represents one of the most reliable attempts to duplicate Warthin's observations, and with negative results.

Many other investigators have experienced similar results. So difficult has it become to demonstrate the presence of spirochetes in lesions of the aortic valve and heart muscle, that many enthusiastic observers are now making a diagnosis of syphilis of the heart muscle on the presence of a few lymphocytes collected around a vessel, or in single rows of five or more. This is risky indeed, as lymphocytes are, notoriously, evidence of a chronic defense reaction in all sorts of disease, and even their perivascular arrangement is by no means pathognomonic of syphilis. Even the finding of isolated or few spirochetes in the heart muscle may mean nothing more than a historical landmark or a resting focus.

While Warthin's observations are of great pathological interest and are very difficult to refute, I am of the opinion that these myocardial lesions have been unfortunately greatly overexaggerated, and that they ordinarily are not extensive enough to produce serious cardiac embarrassment or to explain death. A tendency has been created, especially among clinicians to overemphasize the myocardial lesions and thus distract attention from the aorta.

Bearing in mind the fact that the supporters of the "newer" pathology of syphilis often attribute sudden death to specific myocardial lesions and their results, I have attempted to review my cases, observed as medical examiner of Essex County, over a five-year period, to formulate an opinion as to the correctness of their view.

This I believe is unique because it practically limits itself to bona fide cases of sudden death as encountered by coroners' physicians and medical examiners, and excludes all hospital and institutional deaths, and deaths occurring in a slower manner.

From June, 1925, to June, 1930, my office investigated 8,667 deaths, including homicides, suicides, highway accidents, falls, burns, poisonings, sudden deaths and those cases ordinarily handled by coroners' physicians. Autopsies were performed in 3,325 cases, or 38 per cent.

Of the total number of cases investigated 1,590, or 18 per cent, were cases of sudden death attributed to heart disease. These deaths occurred in the street, while at work, at home, etc., and when unattended by physicians. No hospital cases are included except those dead on arrival. The territory covered by the investigation was Newark and Essex County, having a population of 832,000.

Of the 1,590 sudden deaths hue to heart disease, 300, or 18 per cent, were autopsied. The low percentage of autopsies was caused by the impossibility of removing many cases from their homes and places of death to the morgues, the history plainly indicating that death was due to natural causes.

Rheumatic heart disease was the cause of death in 60 cases, syphilis of the aorta and heart in 101, and arteriosclerotic heart disease in 139 cases.

In 101 cases of sudden death autopsied in which the cause of death was syphilis of the aorta and heart, aortic regurgitation was the predominating lesion in 36 cases, stenosis and atresia of the coronary ostia in 15 cases, aortic aneurysm in 38 cases, and unusual lesions, such as spontaneous rupture of aorta, dissecting aneurysm, miliary aneurysm, etc., in 12 cases.

TABLE I

STATISTICAL SUMMARY OF CASES INVESTIGATED BY THE MEDICAL EXAMINER'S OFFICE DURING A FIVE-YEAR PERIOD (JUNE, 1925, TO JUNE, 1930)

Number of cases investigated		8,667	
Number of autopsies performed		3,325	(38%)
Number of sudden deaths due to heart disease		1,590	(18%)
Autopsies performed	300 (18%)		
Rheumatic heart disease	60 cases		
Syphilis of aorta and heart	101 cases		
Arteriosclerotic heart disease	139 cases		

TABLE II

CLASSIFICATION OF ANATOMICAL TYPES OF SYPHILIS OF AORTA AND HEART ENCOUNTERED IN 101 CASES OF SUDDEN DEATH

Aortic regurgitation	36 cases
Stenosis and atresia of coronary ostia	15 cases
Aneurysms	38 cases
Unusual lesions	12 cases

The age, race and sex of these 101 cases are tabulated in Tables III and IV. It was possible to save for museum purposes about 60 hearts from these cases. Most of the hearts were studied histologically.

TABLE III

AGE, SEX, AND RACE OF 101 CASES OF SUDDEN DEATH FROM SYPHILIS OF AORTA AND HEART

DECADES	10-20	20-30	30-40	40-50	50-60	60-70
Aortic regurgitation 36 cases	0	4	8	16	7	1
Stenosis of coronaries 15 cases	0	2	5	5	3	0
Aneurysm 38 cases	0	2	9	14	8	5
Unusual lesions	0	1	4	5	1	1
Totals		9	26	40	19	7

TABLE IV

	MALE	FEMALE	WHITE	COLORED
Aortic regurgitation 36 cases	30	6	16	20
Stenosis of coronaries 15 cases	12	3	9	6
Aneurysm 38 cases	33	5	17	21
Unusual lesions 12 cases	9	3	4	8
Totals	84	17	46	55

The youngest case in aortic regurgitation was twenty-seven years of age; in coronary stenosis twenty-three years of age, and in aneurysm twenty-four years of age. The oldest individual dying from aneurysm was eighty years of age.

It will be seen from the above that in 101 sudden deaths due to syphilis of the aorta and heart, 55, or over one-half, were in colored people.

The total population covered in this series is 832,000, the colored about 60,000, or over 7 per cent. The greater negro frequency may be explained in two ways: first, the greater prevalence of syphilis among negroes, and second, the fact brought out by Libman that sudden deaths among hyposensitive people are more frequent than in normal and hypersensitive individuals.

Hyposensitive people may collapse and go into shock without feeling pain or other symptoms, while normal, or hypersensitive individuals may rest or seek medical advice at the onset of warning symptoms.

A. AORTIC REGURGITATION—

In the 36 cases of sudden death in which the predominant lesion was an aortic regurgitation, the typical widening of the commissures, deforming lesions of the aortic cusps with thickening of their free edges, and the hypertrophy and dilatation of the left heart formed the outstanding features of these hearts.

The largest heart weighed 1,160 grams, the smallest 360 grams, and the average weight was over 600 grams.

In none of these cases were outstanding myocardial changes noted other than hypertrophy. The little scarring seen in the myocardium was atrophic in type, and due to coronary injury caused by a superimposed arteriosclerosis.

In none of these cases was there an aortic stenosis or organic mitral lesion.

The deforming sclerosis of the aortic valve, with consequent hypertrophy and dilatation of the left ventricle, was of such gross extent that death seemed clearly explained without attributing it to any specific myocardial lesion, which lesion did not exist. It is a well-known fact that hearts of 500 grams or more in weight regularly fail without showing any other evidence of myocardial disease, aside from hypertrophy.

An associated narrowing of the coronary orifices was frequently seen but the outstanding feature of these hearts was the regurgitation.

B. CORONARY STENOSIS AND ATRESIA—

In the fifteen cases of sudden death, in which the predominant lesion was a narrowing of the orifice of one or both coronary arteries, the stenosis or atresia was always due to an encroachment by the syphilitic supravalvular sclerosis over the orifices of the arteries. This process was confined to the aortic wall and did not involve the arteries

distal to the aorta. The lesion was usually in the nature of a sclerotic scar. When there was a definite involvement of the aortic valve, with regurgitation, the heart was much larger than normal. Most of these cases, however, represent pure forms of coronary narrowing with syphilitic aortitis and without regurgitation. The heart, therefore, was normal, or only slightly enlarged.

The largest heart weighed 500 grams, the smallest 250 grams, and the average was about 380 grams.

The coronary arteries beyond the stenosis are usually normal in appearance, and rarely show much superimposed arteriosclerosis.

The myocardium in these cases was usually normal, or showed only slight, or moderate, hypertrophy, and no evidence of specific myocardial lesions was noted. In a few cases the heart was small and the muscle the seat of brown atrophy. I have spoken of this as an inanition atrophy, due to slow cutting off of a considerable amount of the blood supply.

Sudden death in these cases is more difficult to explain than in aortic regurgitation and aneurysm. It is not the same as in coronary sclerosis due to arteriosclerosis where the occlusion takes place rapidly. In syphilis there is a gradual narrowing often to the point of complete atresia. The condition found at autopsy must have existed for months and even years. Compensatory circulation had time to be established, either by way of normal anastomosing vessels, by increased anastomosis between left and right coronary after forty years of age, or by way of anomalous coronary circulation, or by way of the thebesian vessels.

If such a lesion as acute specific myocarditis of any extent could be demonstrated in these cases, the death would be easily explained. We have been unable, however, to find evidence of any extensive myocardial lesions. What then is the mechanism of the sudden death?

Attention has been recently called to the importance of the emotions of excitement, worry, fright, etc., in heart disease and sudden death. One case may be cited as of special interest.

A white man, aged fifty years, was driving his automobile and unwittingly passed a traffic signal. He was severely and unmercifully bawled out by the traffic officer and collapsed over the wheel, dying instantly. Complete atresia of the right coronary was found at autopsy and marked stenosis of the left, with typical syphilitic aortitis. The heart muscle was normal. The stenosis and atresia must have existed for months.

What was the final break that caused death in this case? His wife stated that he had never complained and appeared to be in good health the day he died. It is possible that fright may in the presence of serious chronic lesions, which the individual under ordinary circumstances may get along with in comfort, set up ventricular fibrillation. One of the patients in this series died during coitus.

In none of our cases of sudden death, in which at autopsy a syphilitic stenosis or atresia of the orifices of the coronary arteries was found, have we encountered any evidence of specific myocardial lesions sufficient to explain death, or even to influence the fatal outcome.

Any lesion in the myocardium, besides hypertrophy and occasional brown atrophy (inanition), has usually been interpreted as due to superimposed arteriosclerosis of the coronaries.

C. ANEURYSM OF AORTIC ARCH—

In thirty-eight cases of sudden death, in which a typical aneurysm of aortic arch was found, death is easily explained, as practically all the cases died from rupture.

The heart in the majority of these cases was only slightly or moderately, enlarged. When it was greatly hypertrophied, there was always an added aortic regurgitation, which often was of more recent date than the aneurysm.

The muscle in none of these cases showed serious myocardial lesions that could not be explained by a superimposed arteriosclerosis. In none was there any evidence of specific myocardial lesions sufficient to influence the fatal outcome. As the direct cause of the death is usually rupture, it is obvious that no other factor played an important rôle in the death.

The largest heart in this series weighed 600 grams, the smallest 280 grams, and the average was about 400 grams.

D. UNUSUAL LESIONS—

In 101 sudden deaths from syphilis of the aorta and heart, unusual lesions were encountered in twelve cases.

Spontaneous rupture of the aorta occurred in five cases and was associated twice with bicuspid aortic valve. All the cases were attributed to syphilis of aorta, but it must be admitted that in this lesion the evidence of syphilis is often slight and difficult to determine with certainty. In none was there any narrowing of the isthmus. In two the rupture was complicated by an acute dissecting aneurysm.

Miliary aneurysms of the aorta with small blow-outs, usually into the pericardium, occurred in three cases.

Aneurysm of the right coronary artery was the cause of death in one case, rupturing into the pericardium. This was the only instance of gross syphilis seen in the coronary arteries beyond the aortic wall.

An intimal ulcer was seen in one case.

Negro, aged twenty-four years, collapsed in a lunch wagon. A small patch of syphilitic supravalvular sclerosis was found above the opening of the left coronary artery. This had ulcerated through the intima and had over it a thrombus composed chiefly of blood platelets which occluded the orifice of the coronary in a ball valve fashion, and had caused embolism into lumen of artery. Miliary gummata were found in the spleen, and an old penile scar.

A gumma of the left ventricle, on the interventricular septum, was the cause of one death.

A sudden death due to congenital syphilis of the aorta was seen in one case.

Negro boy, aged ten years, collapsed in street and died instantly. Extensive aortic syphilis indistinguishable from that found in acquired cases was found. The ordinary signs of congenital lues were found.

This is the only case of congenital syphilis of the aorta and heart encountered in this series.

E. SUMMARY—

1. Sudden death in chronic heart disease is commonly due to acquired syphilis of the aorta and heart. Syphilitic heart disease (33 per cent) is next in importance to arteriosclerotic heart disease (47 per cent), which is responsible for the greatest number of cardiac deaths. It exceeds rheumatic heart disease (20 per cent) as a cause of sudden death. Many of the rheumatic cases have a slower death from congestive failure or from superimposed subacute bacterial endocarditis.

2. Sudden death in acquired syphilis of the aorta and heart is almost always due either to an aortic regurgitation or to narrowing or atresia of the coronary arteries, or to the production of an aortic aneurysm, or to any combination of these three great dangers of syphilitic aortitis.

3. Sudden death is occasionally due to unusual lesions such as spontaneous rupture of aorta, dissecting aneurysm, gumma of heart muscle, miliary aneurysm, etc.

4. Specific lesions of the myocardium and of the coronary arteries beyond the aortic wall are infrequent, and, when they occur, are so slight in extent as to be of little practical importance. They rarely embarrass cardiac action, are insignificant in the production of cardiac failure and the slower modes of cardiac death, and are of little importance in explaining sudden death.

5. Congential syphilis affecting the heart and aorta is so rarely encountered that it is of little clinical or pathological importance in the causation of sudden death in chronic heart disease.

PART II

CARDIAC SYPHILIS IS ESSENTIALLY A SUPRAVALVULAR AORTIC SCLEROSIS, ITS MAIN DANGERS BEING AORTIC REGURGITATION, STENOSIS OR ATRESIA OF THE OSTIA OF THE CORONARY ARTERIES AND AORTIC ANEURYSM. ALL OTHER FORMS DESCRIBED IN MEDICAL LITERATURE ARE EITHER OF LITTLE CLINICAL IMPORTANCE, UNCOMMON, RARE, OR DO NOT EXIST

Acquired syphilis of the aorta and heart shows clinical manifestations usually fifteen to twenty years after infection, remaining undiscoverable, hence latent, and apparently harmless during that time.

It may remain latent throughout life and appear only as a historical landmark at autopsy, in the form of a small insignificant scar.

Genuine heart disease due to syphilis usually occurs between thirty-five and forty-five years of age. At least three-fourths of the cases show symptoms between the ages of thirty and fifty-five years. It is a little later than most rheumatic and a little earlier than most arteriosclerotic cases.

A. BIOLOGICAL DEVELOPMENT OF SYPHILIS OF AORTA AND HEART—

We know from the clinical failures to prevent syphilis by early excision of the chancre, backed by considerable experimental data, that there is an early invasion of the blood stream with *Treponema pallidum* even before the initial lesion appears.

The visible chancre appears as a local defense reaction at the original site of infection. The organisms multiply in the initial lesion in enormous numbers and are scattered over the body constantly by two important routes. The first is directly into the blood stream at the portal of entry. The second is a slower route by way of the lymphatics to the regional glands, where many organisms are undoubtedly destroyed by the phagocytic reticulo-endothelial cells lining the lymph sinuses.

The regional lymph nodes (for example the inguinal group) stop the infection temporarily by slowing it up, and the adenitis is purely a defense reaction. Many organisms survive, pass the first barrier of defense, and finally reach the thoracic duct. Eventually they are poured into the venous blood stream and taken to the right side of the heart.

Early treatment may destroy great numbers of spirochetes in and along the slower lymphatic route and in the initial lesion, but it is generally administered too late to destroy organisms which enter the blood stream direct from the portal of entry.

Later, when the secondary rash appears, there is a stage of very pronounced septicemia, or spirochetemia, when treponemata in large numbers invade every tissue of the body accessible to the blood stream. Many are taken to the myocardium.

The stage of septicemia does not last long. Even without treatment the normal organs of filtration and purification of the blood stream rapidly remove circulating treponemata from the blood, and the initial lesion has retrogressed or healed so that no further contamination of the blood stream takes place.

The purification of the blood-containing organs is further hastened by treatment, which is usually instigated before this time. Such early treatment, however, may be disadvantageous because the remaining spirochetes are driven into corners of the body inaccessible to the circulation. Treatment, therefore, must be persisted in over long periods.

As the stage of spirochetemia passes away the various organs attempt to rid themselves of the organisms by way of filtration, by phagocytic properties of reticulo-endothelial cells, and by way of lymphatic drainage into neighboring lymph nodes. This process may take years.

The spleen is greatly aided in freeing itself of organisms by its rich filtering structure, which permits stagnation and destruction by its reticulo-endothelial cells.

The lungs, which, on account of their very great capillary area have received a greater dosage of organisms than perhaps any other part of the body with the exception of the skin, must clear themselves in a somewhat different manner. Many of the organisms pass through the lungs' capillaries and reach the systemic circulation. Many are slowed up in the lungs, and because the *Treponema pallidum* is always attempting to leave the circulation for extravascular tissues in which they are less liable to injury, many escape into the interstitial portions of the lungs.

Numerous extravascular spirochetes may be further phagocyted by even the alveolar epithelium, which are probably mesothelial in origin and a part of the reticulo-endothelial system.

The lungs eventually rid themselves of the organisms by way of their lymphatics which drain to the peribronchial and regional nodes of the mediastinum. These become collecting stations, or reservoirs, for the storage of spirochetes. Here they are exposed to the phagocytic action of the reticulo-endothelial cells of the lymph sinuses.

In certain other organs, particularly the bones, lymph spaces of the skin, the nervous system and the heart muscle, the organisms are apt to rest and remain for years without attempt at removal, and with very little local reaction. In the heart, for instance, there can be no removal by lymphatic drainage, as lymphatic drainage from the heart muscle is scant. These locations are usually inaccessible to the blood stream, and, hence, to treatment.

Does cardiac syphilis begin at this stage? Do the organisms remain there in a latent condition, or do they set up a specific inflammation of the myocardium in the early stages of syphilis?

Warthin's observations lead him to conclude that in the second stage of syphilis there is a very active specific infiltration of the heart muscle.

Clinically, it is well known that various cardiac disturbances take place during the early stages of syphilis, such as tachycardia, bradycardia, arrhythmias and syncope. McLester[6] states that the heart is easily excited and quickly exhausted. He is of the opinion that probably two-thirds of the patients with early syphilis show these functional disturbances. It is questionable whether this condition represents a true myocarditis, which he thinks is rare. Involvement of the

cardiac nerves, the vagus and sympathetic, as well as psychic influences, play a rôle in these disturbances. Brooks[7] thinks that the production of clinical symptoms in this stage is very infrequent. Wile[8] thinks that lesions of the heart are rare in early syphilis.

It is obvious that this question is very important. If there is a specific myocarditis in early syphilis, there is a foundation laid for a specific interstitial gummatous myocarditis, which some claim is so common in later syphilis.

I believe that it is possible to have a specific early myocarditis but that the lesion is very unusual. I also think that the heart muscle filters out many organisms during the secondary stage and they are eliminated with great difficulty. Those surviving often remain for many years without doing appreciable damage.

The finding, therefore, of a few spirochetes in the heart muscle in latent syphilis, perhaps surrounded by a few lymphocytes, may mean nothing more than an insignificant historical landmark. In a similar manner spirochetes may often rest in the skin of latent syphilities, leaving no gross, and little microscopic evidence of their presence. Yet syphilis may be transmitted to rabbits by inoculation.

It is possible, therefore, that later gummatous myocardial lesions may have their origin in these early foci of specific myocarditis, or in the rests of treponema brought to the heart muscle during the early stages of bacteriemia.

Most authorities have for years agreed that the earliest histologic lesions in syphilis involving the aortic root, will be found around the vasa vasorum in the adventitia, where there is a mantle of lymphocytes and histiocytes with an obliterating endarteritis.

It, therefore, seems reasonable to believe that the lesion in early aortic syphilis is a lymphatic extension of spirochetes from the reservoirs in the mediastinal lymph nodes by retrograde lymph flow into the perivascular spaces around the vasa vasorum.

Some years ago, Klotz[9] cited the mediastinal factor in aortic syphilis. He furnished pathological observations, calling attention to the mediastinitis and periaortitis in syphilis of the aortic root and in aneurysms.

In addition, to support the mediastinal theory, there is roentgenographic evidence during life that around aneurysms in particular and widened aortas the seat of luetic aortitis there is a fuzzy border explained only by the periaortitis.

Stokes[10] has further shown that during treatment of an aneurysm by specific drugs, many of the clinical symptoms, especially the pain, are relieved by the melting away of the mediastinal factor, while the physical signs of the aneurysm, such as size, pulsation and murmurs, often become intensified as a result of the relief of the surrounding tense barriers.

While I believe that the mediastinal factor is the important one in explaining the localization of the syphilitic process in the root of the aorta, it is still extremely difficult to prove.

It would be interesting to observe whether experimental transmission to rabbits could be made from mediastinal glands and periaortic tissues. Likewise more accurate data of the lymphatic and vascular supply of the aortic root are needed.

B. CONGENITAL SYPHILIS OF THE AORTA AND HEART—

It is a remarkable fact that with all the discussion about congenital cardiac syphilis the cases observed are very few in number.

Pediatricians in the examination of large numbers of children with undoubted congenital syphilis find almost none in which a diagnosis during life of syphilitic heart disease is possible. Clinicians encounter similar experience in older persons.

At autopsy the pathologist rarely finds any evidence of syphilis of the aorta and heart in cases having other earmarks of congenital syphilis, excluding stillbirths, as well as syphilitic infants dying in the first few months after birth. In the latter, spirochetes can be found in various organs, especially the liver, spleen, lung, osteochondral portions of long bones, and often in myocardium, yet such cases usually die not from heart lesions but from syphilitic meningitis.

In heredosyphilis the child is infected through the placenta, and an incalculable number of treponemata circulates throughout most of the organs, the number having no parallel in acquired syphilis. If the mediastinal theory is correct in the localization of acquired syphilis in aortic root, it might be possible that the aorta escapes in congenital syphilis, because the lungs of the fetus have escaped the large dosage of organisms that the other organs have received due to the fetal circulation not passing to any great extent through them.

In instances in which the lungs receive a large dose, a fatal pneumonia alba often occurs.

C. SYPHILITIC SUPRAVALVULAR SCLEROSIS—

The main and most important lesion in nearly all cases of acquired syphilis of the aorta is a supravalvular sclerosis. Most of the other changes and phases of cardiac syphilis depend upon this lesion.

The earliest lesions are microscopic and occur around the vasa vasorum in the adventitia of the root of the aorta where there is seen a collection of lymphocytes and histiocytes, lying, probably, in the perivascular lymph spaces. Stained sections may show spirochetes in these areas, but usually they are found with difficulty. Small, miliary gummata are formed in the adventitia.

There follows a secondary invasion of the media with consequent breaking up of elastica and weakening of the vessel wall. Obliterating endarteritis of the vasa vasorum is a common finding. Syphilis has

been usually considered a disease of the small arteries. The obliterating endarteritis is held by many to be a primary lesion indicating a hematogenous entrance of the syphilitic virus. Syphilis, therefore, being an endarteritis of the small vessels, it is obvious that it would appear at the place which contains the most small vessels, and this is the root of the aorta. This portion is also more richly supplied with lymphatics.

My interpretation of the endarteritis has been different, although it is not, as yet, subject to finality. Instead of assuming that the intimal changes indicate that the primary effect has been upon the interior of the vessel, hence a hematogenous infection, I have been in the habit of assuming that the vessels become obliterated as a part of a defensive reaction to an inflammation which starts around and external to them. It is an attempt to heal the surrounding gummatous area by limiting its blood supply, producing necrosis, etc.

The lesion develops to a stage at which it can be recognized with the naked eye. It usually begins in the aortic wall, just distal to the attachments of the aortic cusps. The earliest patch is often triangular, and situated just above the commissures connected with the aortic cusp forming the sinus of Valsalva, where the left coronary has its origin. The base of the triangle is usually pointed distally. There is a gray or slightly yellowish elevation with steep sharp edges, smooth on top, or marked by shallow furrows separating trivial secondary elevations.

The process spreads in a horizontal manner around the root of the aorta and distally as far as the mouths of the great vessels springing from the aortic arch. The orifices of the great vessels of the arch may often be narrowed to a marked degree. It may diffusely involve the whole aortic arch. Separate processes may develop in a similar manner in the thoracic or even abdominal aorta.

Histological study shows that the gummatous process, starting and most pronounced in the adventitia, has infiltrated the media, breaking up and pushing aside elastic fibers, and has gained access to the subintimal tissue of the aorta where there is less resistance to further infiltration.

I am not satisfied that the extension of the process follows the vessels down into the aortic cusps but rather am inclined to think it follows tissue spaces of least resistance and along perivascular lymph spaces.

The location of the triangular patches above the commissures, or their commissural origin, is best explained by the tug at these places during pulsatory dilatation of the aortic root, and the strain put on the valves and wall of the aorta when the ends of the free margins come together.

I speak of the whole process as a sclerosis because the lesion found at autopsy is in the nature of a deforming defect which has followed and is following a previous gummatous infiltration. Two groups, however, must be recognized. In one the process is distinctly softer, and histological examination still shows quite an active process. Such cases can be greatly benefited by treatment. In the other the gummatous process is subsiding so that the sclerosing deformities are more pronounced and predominate. This latter is the most frequent type seen at autopsy.

Symptoms and Physical Signs of Early Supravalvular Sclerosis.—The symptoms produced by early aortitis are chiefly dyspnea, which is mild, or slight on exertion, or comes in nocturnal paroxysms.

Precordial distress usually above the third rib is common.

Early physical signs are due to surrounding periaortitis and mediastinitis, which produce dilatation of the aorta without any intimal lesions being present.

The most characteristic and valuable physical sign is an accentuated second aortic sound, which is ringing and bell-like in quality. Such a finding in a man between thirty and forty-five years of age, without evidence of arteriosclerosis, hypertension or rheumatic heart disease, should force one to exclude syphilis by using every available means. The diagnosis of aortitis is difficult, and the disease is rarely recognized in the early stages. The blood Wassermann is often negative, and if we depend upon a serological diagnosis of cardiac syphilis we will miss some 30 per cent of cases.

In addition, a soft, systolic murmur may often be heard over the aortic area. This murmur is not transmitted and is probably produced by the increased rigidity of the aortic tube, since at this time no endocardial lesions may be present.

D. SYPHILITIC SUPRAVALVULAR SCLEROSIS MASKED BY SUPERIMPOSED ATHEROMATOSIS AND ARTERIOSCLEROSIS—

One of the most confusing factors in the diagnosis of syphilis of the aorta and heart at autopsy is that the syphilitic lesion may be often masked by a superimposed atheromatosis, or arteriosclerosis, so that the underlying syphilis may be completely obscured.

This is so common that the greatest care must be exercised so that myocardial lesions due to coronary injury from the ordinary garden variety of senile arteriosclerosis are not mistaken for syphilis.

Pure, uncomplicated syphilitic lesions in the aorta are characterized by the presence of little or no fat and no calcification.

Infantile atheromatosis is very common. Yellowish plaques on the aortic cusp of the mitral are frequently seen in infancy. Atheromatous plaques in the coronary arteries may be seen as early as one year, and often in the second decade of life. The summit of cardiovascular life is about forty-five years of age when man has reached his biological

usefulness as far as reproduction of his race is concerned. After forty-five nature is trying to dispose of him rapidly as his usefulness is over. It is not only common to find evidence of atheromatosis and arteriosclerosis after the forty-fifth year, but unusual not to find it. Coronary thrombosis which is practically always due to localized arteriosclerosis of the coronary arteries is really a disease of early middle life and occurs most frequently around the summit of cardiovascular life, in contradistinction to the belief of many that it occurs later.

While we believe that cardiac syphilis forms only about 10 per cent of chronic organic heart disease, this assumption is based chiefly upon the finding of gross lesions characteristic of syphilis at autopsy. In the series of sudden deaths syphilis formed about 33 per cent of chronic organic heart disease producing death.

When we remember that many cases of cardiac syphilis may be obscured at autopsy by the arteriosclerotic process, it is evident that we miss many cases, and the incidence may be much higher.

Again, if we accept the criteria laid down by Warthin for the histological diagnosis of syphilis of the heart, the incidence will very rapidly increase.

It is quite impossible to state the frequency of severe syphilitic lesions of the heart causing death and the incidence of latent syphilis of the heart.

It is also important to state here that in uncomplicated syphilitic aortitis there is no marked hypertension. In this respect I have been for years of the opinion that syphilis played no rôle in the production of essential hypertension.

Furthermore, I am not willing to admit that persons suffering from syphilis of the heart and aorta are more liable to a superimposed arteriosclerosis.

E. SUPRAVALVULAR SYPHILITIC SCLEROSIS EXTENDING DOWN ON AORTIC VALVE WITH THE PRODUCTION OF REGURGITATION—

Aortic Regurgitation.—Aortic regurgitation is the first and most important danger of supravalvular sclerosis (syphilitic aortitis).

In a combined series of deaths, including hospital cases, aortic regurgitation occurred in about 60 per cent of cases of luetic aortitis which resulted in death.

In a series of 101 sudden deaths from cardiac syphilis, excluding hospital cases, aortic regurgitation was found as the cause of death in 36 per cent of cases. This shows that while the insufficiency is a very important lesion in sudden death a great many patients die a slower death from cardiac failure of the congestive type.

The aortic cusps are not primarily involved in acquired syphilis, but the regurgitation always results from a previously existing supra-

valvular lesion which has infiltrated to spread the cusps eventually, or to involve them in the syphilitic process.

The consecutive pathological events in the formation and development of aortic regurgitation, together with their clinical symptoms, may be discussed together.

Supravalvular Sclerosis.—The process in the aorta has already been discussed.

Extension to Aortic Cusps.—Extension of the syphilitic gummatous process through the media into the subintimal spaces producing the triangular patches, continues in the direction of the attachment of the aortic cusps, usually following the lines of least resistance, which is alongside of and between the fan-shaped subintimal fibers, the remnants of those fibers forming originally the aortic cusps.

The result is a pushing apart of the cusps at their attachments by the gummatous and sclerosing process. Sometimes the attachments of the cusps may be separated by at least 1 cm. Often, just a furrow exists between the attachments of the adjacent cusps, which are thickened and infiltrated. This widening of the commissures is the earliest sign of aortic regurgitation, and is practically the main factor in its production.

Clinical Symptoms and Physical Signs of Early Involvement of the Aortic Valve.—Extension to the aortic cusps causes a change in the systolic murmur. The murmur is thereby transmitted down the left border of the sternum, and as the cusps become involved, it becomes rough and harsh and transmitted into the vessels of the neck.

Widening of the aorta to percussion, fluoroscopic and roentgenographic examination may, or may not, be detected at this time. A slight hypertenson is the rule in well developed, pure forms of aortic syphilis, the systolic pressure being 135 to 150 to 155. There is not sufficient hypertrophy of the left heart to detect usually at this period.

Involvement of the Aortic Cusps.—A continuation of the process down the attachment of the cusps takes place and often occurs across their free edges.

Fibroblasts lay down collagenous fibers. A hyalinized ball-like edge results. While, of course, considerable round-cell infiltration of a specific nature is seen in the free edges of the cusps near their attachment, the portions between the free edges are often remarkably clear of such specific changes. As many cases of regurgitation due to syphilis are seen which show no thickening of the free edges, but only widening of the commissures, I am inclined to interpret the thickening of the free edges as mainly mechanical in nature and due to strain produced by the regurgitant blood stream.

Dilatation of Aortic Ring.—The production of regurgitation by dilatation of the aortic orifice is not of much importance.

Aortic Valve Incompetent.—The distorted, thickened, rolled, and retracted aortic cusps with the widened commissures produce irreparable damage to the valve.

Subendocardial Fibrosis.—From trauma of the regurgitant blood stream, subendocardial fibrosis over the interventricular septum below the aortic valve, with the production of the so-called bird's nests, false bands and cusps, often takes place. The lesion is characteristic of a regurgitation but is not pathognomonic of syphilis. It is purely of mechanical origin and has nothing to do with any specific inflammation.

Hypertrophy of Heart, Especially Left Ventricle.—Hypertrophy of the muscle of the left ventricle is usually the only gross and microscopic finding of any importance. All other myocardial lesions are usually due to a superimposed arteriosclerosis. Occasional areas of specific myocarditis, especially in region of aortic ring may occur, they are usually small in amount, difficult of interpretation and of insignificant import.

Symptoms and Physical Signs of Fully Developed Aortic Regurgitation.—The symptoms and physical signs of a well-developed aortic regurgitation need not be repeated here.

Dilatation of Left Ventricle.—This represents about the last lesion in a well-developed case.

Death in Aortic Regurgitation.—Death in aortic regurgitation is in over half of the cases due to cardiac failure of the congestive type, therefore, a slow one.

Sudden death is common, occurring from acute cardiac dilatation or from cardiac failure of the anginoid type. The latter is especially liable to occur when there are associated lesions about the orifices of the coronaries, or a superimposed coronary arteriosclerosis.

Patients with well-developed aortic regurgitation due to syphilis do not usually survive a two-year period after the diagnosis has been made, even when properly treated. Many die in six to twelve months. Exceptional cases, however, may live for many years.

F. SUPRAVALVULAR SYPHILITIC SCLEROSIS WITH ENCROACHMENT ON THE ORIFICES OF THE CORONARY ARTERIES—

Coronary Stenosis and Atresia.—Narrowing of the orifices of the coronary arteries is the second important danger of supravalvular sclerosis (syphilitic aortitis).

In a combined series of deaths, including hospital cases, stenosis or atresia of the coronary ostia occurred in about 30 per cent of cases of syphilitic aortitis which resulted in death. As many of the aortic regurgitation cases also have narrowing of the coronaries, an exact grouping is quite impossible.

In a series of 101 sudden deaths from syphilis of the aorta excluding hospital cases, stenosis or atresia of the coronary orifices was

found to be the cause of death of some 15 per cent. Most showed little or no regurgitation.

The consecutive pathological events leading to narrowing of the coronary ostia with their symptoms are as follows:

Supravalvular Sclerosis: The primary lesion is of course the supravalvular sclerosis.

Stenosis and Atresia of Coronary Ostia: An important observation which attracted little attention in the causation of coronary narrowing in these cases was made by von Glahn,[11] who showed that often one or both coronaries may have their origin above the sinuses of Valsalva. Such high placed coronaries are a frequent congenital anomaly.

Martland[12] called attention in 1927 to the clinical importance of this observation and also to the comparative freedom of involvement of the sinuses of Valsalva in the syphilitic process.

As syphilitic supravalvular sclerosis usually starts in the portion of the aorta above a base line drawn through the upper limits of the attachments of the aortic cusps, coronary arteries which are congenitally situated above this line are especially liable to scarring of their ostia, while those normally arising in the sinuses often escape encroachment.

It is unusual for the syphilitic process to be seen in larger branches of the coronaries, and syphilitic coronary disease is practically limited to a narrowing, or atresia, of their orifices by the lesion in the aortic wall.

The heart in these cases is of normal size or only slightly or moderately enlarged.

The right coronary seems to be more liable to narrowing than the left.

When a coronary is completely obliterated so that its opening cannot be found, its exact location can be usually determined by opening the artery distal to the aortic wall. The vessel will usually be found quite normal in appearance and seems to escape a superimposed arteriosclerosis, as the walls have been saved from the wear and tear of arterial strain for some time.

G. SUPRAVALVULAR SYPHILITIC SCLEROSIS WITH PRODUCTION OF AORTIC ANEURYSM—

Aortic aneurysm is the third main danger of supravalvular sclerosis (syphilitic aortitis).

In a combined series of deaths, including hospital cases, aneurysm of the aorta occurred in about 10 per cent of the cases of syphilitic aortitis resulting in death.

In a series of 101 sudden deaths from cardiac syphilis, excluding hospital cases, aortic aneurysm was the cause of death in thirty-seven cases, or about 37 per cent.

The large increase in its incidence in cases of sudden death is easily explained by the mode of death, which is usually rupture.

For many years I have maintained that the heart in aortic aneurysm is not usually enlarged unless there is a coexisting aortic regurgitation.

The consecutive events in the production of aneurysm together with the symptoms may be discussed together:

Supravalvular Sclerosis.—The primary lesion is a supravalvular sclerosis which weakens the aortic wall so that an aneurysm may take place.

Failure of the Sclerosis to Involve the Aortic Valve.—In the formation of most aneurysms the most important factor is failure of the syphilitic sclerosing process to pass downward to the aortic cusps. At autopsy a great many specimens of aortic aneurysms will show little or no involvement of the aortic valve and no regurgitation. The heart is not much larger than normal.

As many aneurysms may exist for from ten to fifteen years, aortic regurgitation is often superimposed upon the lesion as a later development. Occasionally the aneurysm is so near the aortic ring or so large that it may cause regurgitation by dilatation of the ring alone, but this is not common.

What, then, is the mechanical factor that produces aneurysm? In uncomplicated syphilis there is only a slight or mild hypertension. The systolic blood pressure in aortitis ranges from 135 to 155 mm. In aneurysms the range is even lower. The production of aneurysm is more likely to occur if the aortic valve is competent, and the maintenance of a high diastolic pressure against the weakened aortic wall is possible.

Aneurysmal Dilatation.—From its inception the dilatation usually becomes progressively worse through the constant effect of the high maintained diastolic pressure.

Thrombosis.—The endothelial lining of the aneurysmal sac or dilatation is soon lost in places. Thrombus forms with organization and typical lamination. This has often been a protective influence, as many layers of laminated clot may act as a tampon. Even after rupture it may temporarily seal the small opening. The following case is of interest:

A white male, aged forty-five years, in apparent health had a terrific hemoptysis from which he collapsed. His recovery took about two weeks. Fluoroscopic examination showed a large aneurysm of the arch. He was living six months after the rupture. A sliding clot must have temporarily sealed the small blowout.

Pressure on Neighboring Structures.—This condition is common and causes many of the classical signs and symptoms of aortic aneurysm. They need not be discussed here. One interesting and unusual condition is the so-called aneurysmal phthisis of Osler. Pressure on a main bronchus may cause extensive suppurative bronchitis with abscesses of the lungs, etc. A septic type of temperature and scattered

physical signs of lung infection, with emaciation, may lead to the diagnosis of pulmonary tuberculosis.

Erosion of Adjacent Structures.—In this respect the erosion of the bodies of the vertebrae are of interest, particularly the resistance to erosion offered by the elastic intervertebral discs. These discs often remain intact, projecting out between the eroded bodies.

Symptoms.—The symptoms and physical signs of aneurysm are well known.

Death in Aneurysm.—As stated, sudden death in aneurysm is almost always due to rupture. If the orifices of the coronaries are also stenosed, death may be sudden from cardiac failure of anginoid type.

Slow death is due to failure of the congestive type, or a result of pressure on surrounding structures.

Occasionally death may result from embolism from contents of aneurysmal sac. Rupture into a tuberculous lymph node may disseminate tubercle bacilli producing a fatal miliary tuberculosis.

H. TREATMENT—

It is perhaps excusable for a pathologist to discuss treatment if he has formed certain opinions based upon anatomical observations.

Supravalvular Sclerosis.—Intensive treatment is desirable and should be given in early aortitis when there are no coronary, myocardial or cerebral signs or symptoms.

Of greatest importance before treatment is undertaken is the condition of the heart and coronary arteries. To determine whether the coronary arteries are involved electrocardiography is invaluable and should always be employed.

The patient must be questioned concerning cardiac pain and anginoid attacks.

Anginoid attacks occur chiefly in those cases in which there is a narrowing of the coronary arteries. As some 70 per cent of cases escape coronary narrowing this is the reason why anginal attacks are not seen with the same frequency as they are in arteriosclerosis.

Often the pain is a typical angina indistinguishable from that due to arteriosclerosis. In rare cases it may simulate an occlusion.

More frequently, however, the pain is not characteristic, and as many of the cases occur in hyposensitive individuals, especially in the negro, other symptoms may replace the pain.

Instead of typical anginal attacks, therefore, there may be only marked weakness, aerophagy, burning or gnawing pain in the epigastrium, symptoms which have little or no relation to exertion and are not relieved by nitroglycerine.

By intensive treatment we mean a period of previous desensitization of the latent syphilitic with mercury, bismuth, iodides, etc., in order to avoid a Herxheimer reaction. This is followed by the administration with great care, of a course of intravenous arsphenamine or any

of its derivatives followed by intramuscular injections of bismuth, etc., and such a course repeated after suitable rest periods according to the progress of the individual case.

If the aortic lesions happen to be soft and predominantly gummatous, which some are, almost a complete healing may be obtained, saving the patient from coronary stenosis, regurgitation, aneurysm, or any combination of these lesions.

If the aortic lesion is more sclerotic in type, which the majority are, the melting away of the sclerotic process can never be completely accomplished, but the disease can undoubtedly be arrested.

With careful treatment cases may often be practically cured provided the lesion has not reached the openings of the coronary arteries. The sclerosis at least stands a good chance of being changed from a slowly progressive disease with a fatal outcome into a stationary one not incompatible with many years of life. A *restitutio ad integrum* is impossible but further progress of the disease may be checked.

Aortic Regurgitation.—Intensive specific treatment is of little value and is distinctly dangerous. If it does not kill the patient, it gives little relief or benefit.

If cardiac failure of the congestive type is present, specific treatment is out of the question, as cases should not be treated during decompensation. Rest, digitalis, and the orthodox treatment for cardiac failure are to be employed.

Mild preparatory treatment with bismuth, iodides, etc., followed by the judicious use of neoarsphenamine in small doses often prolong life. But the results are less brilliant than in any other form of cardiac syphilis. It must be remembered that the patient is suffering from an irreparable, sclerotic valvular defect and that very little pathological basis exists to warrant any wonderful therapeutic results.

Coronary Stenosis.—If in cardiac syphilis narrowing of the coronary arteries is diagnosed with a fair degree of certainty from the clinical history of syphilitic anginal attacks and electrocardiographic evidence, antisyphilitic treatment is usually contraindicated. If treatment is decided upon, the greatest care must be taken to prepare the latent syphilitic properly for arsphenamine or its derivatives.

Too early an injection may be followed by a Herxheimer reaction with edema of the coronary orifice and sudden death, or a severe attack of cardiac pain with all its consequences.

Intensive use of arsphenamine or its derivatives may cause too rapid healing of the syphilitic process and leave a stenotic scar. The effects of a healed lesion may leave the patient in a worse condition than before treatment (therapeutic paradox of Stokes). The following case is cited as an example:

Male, white, aged forty-three years, who was an old luetic for many years, developed a syphilitic laryngitis with almost complete loss of voice. Blood Wasser-

mann negative. Examination failed to show any evidence of involvement of the nervous system, the heart or other organs. He was in good physical condition. No electrocardiographic examination was made. He was started at once without any great amount of preparation, because of the desirability of rapidly clearing up his throat, with intensive arsphenamine treatments. Just after completing his first course he had an attack which resembled a coronary occlusion, with typical drop in blood pressure, shock, extreme and prolonged pain and sudden enlargement of liver. He gradually recovered and had two other similar attacks of less severity. Since this time he has been in fair health except for slight dyspnea. Since his initial attack five years ago his electrocardiograms have shown T-wave negativity in Lead I, abnormal QRS complexes, low amplitude in Lead II, and left axis deviation.

In this case there seems to be little doubt that the orifice of the right coronary was too rapidly healed by intensive treatment, and he has developed a stenosis or complete atresia of the artery due to a healed lesion, the slow course of which allowed compensatory circulation to take place.

Aneurysm.—Many cases of aneurysm, especially those in which there is considerable periaortitis and mediastinitis may be greatly benefited by specific treatment.

The patient should always be prepared as in case of any latent stage of syphilis. Then small doses of the arsphenamines, or their derivatives, carefully administered, with no attempt to cure the disease, may relieve the main symptom, pain, by melting away the surrounding syphilitic periaortitis. Aneurysms, with considerable fibrotic changes, are not so benefited. The treatment is dangerous in aneurysms with thin walls. While the pain is often relieved, the physical signs may increase because of a relief of the surrounding syphilitic inflammation.

In general the effects of antisyphilitic therapy are not altogether favorable, especially when the disease has reached the more advanced stages. Prevention is better than an attempted cure. If syphilis is more effectively treated in the early stages, many cases of aortitis could be prevented.

I. UNUSUAL LESIONS—

Spontaneous Rupture of Aorta.—Spontaneous rupture of the aorta without any relation to trauma is often, but not always, due to syphilis. It is of great medicolegal importance, because the gross evidence of syphilis is often very slight, the aorta and aortic valve being unusually normal in appearance. Frequently, however, histological examination in the region of the tear will verify the diagnosis of syphilis.

The location of the tear is generally about 2 to 3 cm. above the aortic cusps, or in the region of the ductus Botalli. At these locations fixed points exist between the ascending aorta and the pulmonary artery and at the site of the obliterated ductus arteriosus.

These spontaneous ruptures do not always kill and can sometimes be identified at autopsy as a healed scar.

In addition, many of the dissecting aneurysms found at autopsy and appearing as the double barreled aortas, the false tube being entirely lined by ingrowing intima, probably had their origin years before in a spontaneous tear.

The following cases are of interest in connection with the foregoing:

A negro, aged forty-five years, in apparent health, collapsed on the street and was removed to hospital, dying en route. The whole time consumed from the fall on the street to his death was not over thirty minutes. At autopsy a spontaneous rupture of the first portion of the aorta was found with a dissection of the greater part of the adventitia from the entire aorta down to the right femoral artery with tearing into the right and left common iliac arteries and a reestablishment of the blood stream. A final break into the pericardium caused death and prevented a chronic dissecting aneurysm. Many of the intercostal and lumbar arteries were torn completely across between the media and adventitia.

There is no question that in this case almost the entire adventitia was peeled off the aorta in less than thirty minutes.

A white woman, aged forty-six years, collapsed while at work. She was removed to hospital where she lived six hours in a condition of profound shock. At autopsy a spontaneous rupture of the first portion of the aorta was found with a dissecting aneurysm which reentered the aorta just below the innominate artery. A rupture into pericardium caused death.

It is possible, therefore, that many chronic dissecting aneurysms are not of slow progressive origin, but that the greatest extension of the aneurysm takes place at the time of the spontaneous rupture. With reestablishment of the circulation the strain is relieved, death prevented, and healing over a longer period of time takes place.

Miliary Aneurysm.—Small aneurysms of the aorta with minute blowouts usually into pericardium are occasionally seen. They are apt to occur in the first portion of the aorta, frequently near the sinus of Valsalva, or in them.

Other Lesions.—Other lesions than those described above are exceedingly rare and of little importance.

SUMMARY

1. Acquired cardiac syphilis is essentially a supravalvular sclerosis which may manifest itself in one or more of the following ways:

(a) As small isolated patches of sclerosis in locations doing little damage (historical landmarks).

(b) As larger areas of sclerosis which become confluent and convert the aortic arch into a thickened, rubbery tube.

(c) As triangular patches of sclerosis which infiltrate between the commissures of the aortic cusps causing regurgitation.

(d) By extension of the scarring process over the coronary ostia with narrowing or complete atresia of one or both arteries.

Fig. 1.—Aortic regurgitation, First, most frequent and important danger of syphilitic supravalvular sclerosis (syphilitic aortitis). Occurs in about 60 per cent of syphilitic aortitis which result in death (combined hospital and medical examiner's statistics).

About 36 per cent of cases of sudden death due to syphilis of aorta and heart show regurgitation as the predominating lesion (medical examiner's statistics).

SUMMARY:

1. Always a secondary extension from a syphilitic aortitis.
2. Widening of commissures by infiltrating, sclerotic process is the important lesion producing the regurgitation.
3. Thickened free edges of aortic cusps are usually mechanical in origin.
4. Aortic regurgitation is often combined with narrowing or atresia of the coronaries, and it is sometimes superimposed upon an old aortic aneurysm.
5. Heart nearly always shows marked hypertrophy and often dilatation, especially of the left ventricle.
6. Main myocardial lesion is hypertrophy. Seen on gross and microscopic examination. Other lesions are infrequent and of no great significance.
7. The irreparable sclerotic lesion is not as a rule favorably influenced by specific treatment.
8. Sudden death is due to acute dilatation or to an anginoid type of failure when the coronaries are involved. When death is delayed it is usually due to failure of the congestive type.
9. As a rule patients do not survive a two-year period after the diagnosis is made. Many die within six to twelve months. Exceptional cases may live for many years.

Case CME, 9053.—Male, aged 43 years. Colored actor, sudden death while reading his lines.

The heart weighed 1160 grams. Typical, triangular patches of supravalvular sclerosis with extension to the aortic cusps may be noted. There is not much thickening of the free edges of the cusps, the main lesion being the commissural widening.

The heart muscle showed enormous hypertrophy, and no specific lesions were seen on microscopic examination. The right coronary has a high origin and shows beginning encroachment on its orifice.

A probe is inserted in the orifice of the left coronary.

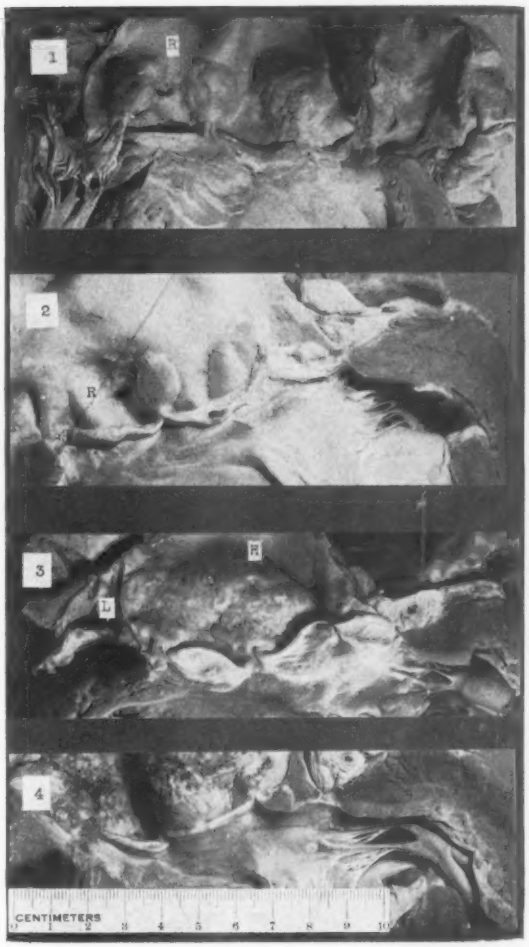

Fig. 2.—Aortic regurgitation. (*1*) CME, 2543. Male, white, aged thirty-five years. Sudden death in moving picture house. The typical triangular patches of sclerosis with extension to the aortic cusps, widening of the commissures, thickening of free edges, retraction of cusps and false bands on interventricular septum, may be noted. The coronaries, although their orifices are high, have escaped encroachment by the syphilitic process. The sinuses of Valsalva are free. The orifice of the right coronary is on the edge of a sclerotic patch but it is not yet stenosed.

(*2*) CME, 4644. Male, colored, aged forty-six years. Sudden death in physician's office. Same as *1*. There is beginning encroachment on orifice of right coronary which is situated slightly above base line.

(*3*) CME, 4813. Male, colored, aged thirty-eight years. Sudden death on street. The heart shows aortic regurgitation combined with coronary stenosis and atresia. There is fusion of the triangular patches forming a horizontal band across first portion of the aorta and producing complete atresia of the right coronary, the orifice of which is an atresed dimple 1.5 cm. above the base line. There is marked rolling of the free edges of the cusps.

(*4*) CME, 4532. Male, white, aged fifty-seven years. Sudden death while at work. The heart shows aortic regurgitation with marked superimposed arteriosclerosis. The aortic cusps are retracted, shrunken with marked rolling of their edges. The syphilitic process in the aorta is almost entirely obscured by the arteriosclerosis.

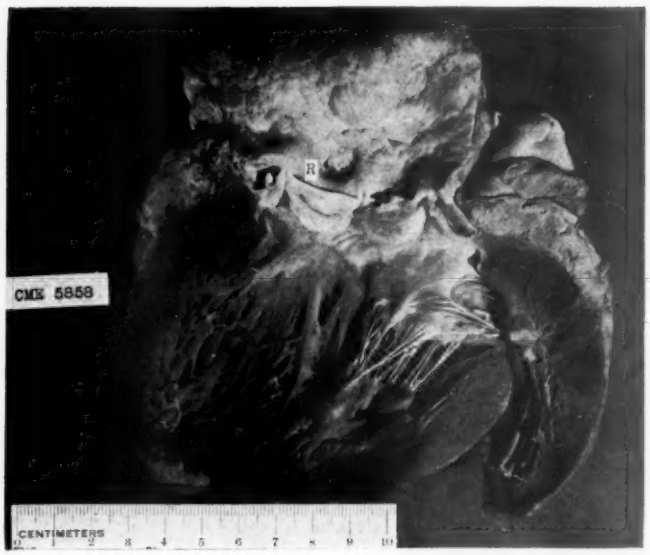

Fig. 3.—Stenosis and atresia of coronaries, second main danger of syphilitic supravalvular sclerosis (syphilitic aortitis). Occurs in about 30 per cent of syphilitic aortitis resulting in death (combined hospital and medical examiner's statistics). This percentage, however, includes many cases of aortic regurgitation with combined lesions.

About 15 per cent of cases of sudden death due to syphilis of aorta and heart show coronary stenosis and atresia in more or less pure form.

SUMMARY:

1. The process is always a narrowing, often to a complete atresia, of one or both arteries, due to encroachment upon their orifices in the aortic wall by the syphilitic process. Syphilis of larger and even smaller branches of the coronaries is rare and of little clinical or pathological importance.

2. If the coronary orifices are congenitally high above a base line drawn through the upper attachments of the aortic cusps, they are much more liable to narrowing than if they arise normally in the sinuses of Valsalva.

3. The heart is usually normal in size or slightly enlarged in the pure forms of this lesion. The muscle is quite normal in appearance and usually shows no evidence of any specific myocardial lesions. Occasionally an inanition atrophy similar to brown atrophy is seen.

4. As the narrowing or atresia takes a long period of time in its development, compensatory circulation is often established.

5. Sudden death is difficult to explain on account of the long duration of the stenosis. Physical strain, fright, emotions, etc., seem to play an important rôle. Syphilitic angina usually occurs in this type of case and not in other forms of cardiac syphilis. It is usually anginoid with atypical symptoms, but sometimes resembles the angina of arteriosclerosis, and even an occlusion in rare instances.

6. Specific treatment in these cases is usually contraindicated, because of the danger of a Herxheimer reaction or too rapid healing causing a therapeutic paradox.

Case, CME, 5858—Male, white, aged forty-nine years. Sudden death on street. The heart shows extensive, diffuse supravalvular sclerosis with complete atresia of the left coronary, the orifice of which cannot be found, and marked stenosis of the right coronary. Both arteries have their origin above the base line.

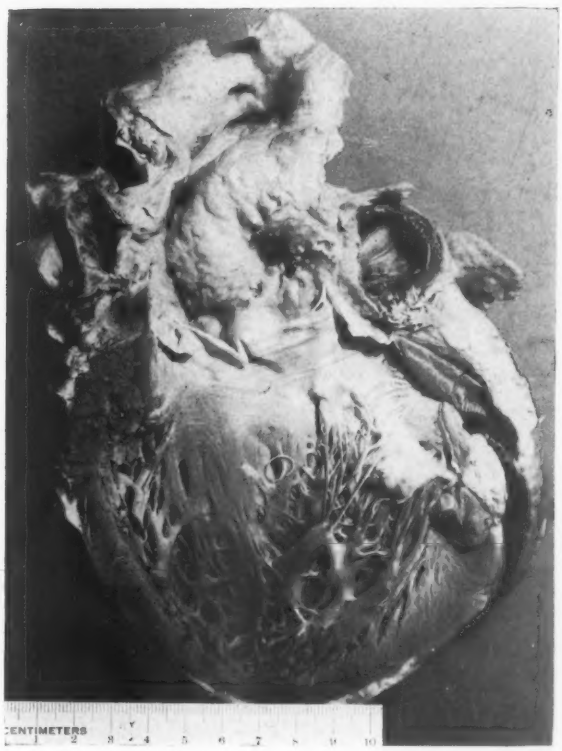

Fig. 4.—Aortic aneurysm, third main danger of syphilitic supravalvular sclerosis (syphilitic aortitis).

Occurs in 10 per cent of cases of syphilitic aortitis resulting in death (combined hospital and medical examiner's statistics).

About 37 per cent of sudden deaths due to syphilis of the aorta and heart are caused by ruptured aneurysm.

SUMMARY:

1. The aneurysm is due to weakening of the aortic wall by the syphilitic, gummatous infiltration. A high maintained diastolic pressure, when the aortic valve is not involved and there is no regurgitation, is the main cause of the aneurysmal dilatation.

2. Cases of long duration are frequently associated with a regurgitation which has been superimposed after the aneurysm has existed for some time.

3. If there is no regurgitation and the aneurysm is not near enough to the aortic ring to produce dilatation, the heart is usually normal in size or only moderately hypertrophied.

4. Death is usually sudden and due to rupture. If the coronaries are involved it may be sudden with or without anginoid symptoms. Slow death is due to failure of the congestive type, or is a result of pressure on surrounding structures.

5. Pain, the main symptom, can often be relieved by proper specific treatment, although the physical signs may increase. Specific treatment is less dangerous and gives better results than in regurgitation or coronary stenosis.

Case, CME, 3560. Male, white, aged forty-eight years. Sudden death in street. A small sacculated aneurysm of the first portion of the aorta may be noted. The surrounding aorta is the seat of a diffuse supravalvular sclerosis. There has been no encroachment on the orifices of the coronaries in this case. Slight widening of the commissures is seen, but the aortic valve is still competent. The heart is practically normal in size and the muscle is not affected. Sudden death due to rupture into pericardium.

(e) By weakening of the aortic wall and production of aneurysm. This is especially likely to occur when the aortic valve remains competent.

(f) By any combination of the above.

2. We speak of the process as a sclerosis because the lesion found at autopsy is a deforming defect which has been following previous gummatous infiltration. In a somewhat similar manner we speak of the chronic valvular defects of rheumatism. The process in syphilis never heals completely. In some cases the lesion may remain distinctly gummatous and the involved areas soft. These are more favorable for treatment than the deforming sclerotic cases.

3. Syphilis involving other portions of the heart is unusual and is of no great clinical or pathological importance.

CONCLUSIONS

1. From a clinical and pathological standpoint, I believe that we should regard syphilis of the aorta and heart as an acquired disease (congenital cases being infrequent) developing insidiously and showing symptoms years after the initial infection.

2. It is possible to recognize clinically and to diagnose an early aortitis, an aortic regurgitation, a narrowing of the coronary ostia, an aneurysm, or any combinations of these lesions. Treatment and prognosis should be based mainly upon such recognition.

3. The myocardium in syphilis is frequently normal. When the aortic valve is involved, the main myocardial lesion is hypertrophy. Inanition atrophy is occasionally encountered. Specific lesions of the myocardium are infrequent, and, when they occur, are so slight in extent as to be of little practical importance.

4. It is safer and better to assume that the coronaries distal to the aortic wall are usually normal in pure, uncomplicated syphilis, and that coronary occlusions, anemic infarcts, necrosis of heart muscle, replacement fibrosis, aneurysms of ventricular walls, and fibrous myocarditis are almost entirely due to coronary injury dependent upon an arteriosclerotic process and have nothing to do with syphilis. That rheumatism and other infections may also produce forms of interstitial myocarditis is obvious. But it appears that syphilis does not play an important rôle in the production of such lesions.

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DISCUSSION

Dr. R. W. Scott, Cleveland, Ohio.—I am interested in this material. I would like to ask Dr. Martland in regard to those cases in which arteriosclerosis obscures the lesions of aortic syphilis, whether or not he believes that widening of the commissure affords sound evidence for the presence of syphilis. We agree with his observation concerning involvement of the valve, especially the middle portion. We have not demonstrated syphilis in this position, and I think that the thickening of the midportion of the valves is due to eversion during diastole.

Dr. H. S. Martland (closing).—I think the widening of the commissure is so characteristic of syphilis as to be almost sufficient for diagnosis.

THE GROSS PATHOLOGY OF THE HEART IN CARDIOVASCULAR SYPHILIS

JAMES G. CARR, M.D.
CHICAGO, ILL.

THIS study covers cases from the records of the Cook County Hospital in which a diagnosis of syphilitic aortitis was made at autopsy. Except for 8 cases, the full clinical records of which for one reason or another could not be obtained, all of the cases are here included in which syphilitic aortitis was found during 1929.

The diagnosis of syphilitic aortitis was based on accepted macroscopical and microscopical findings of this condition. Syphilitic aortitis is characterized grossly by its appearance and location. The intima of the aorta shows an irregular wrinkling, fine or coarse, with irregularities of the surface, the result of elevations and depressions produced by scattered areas of inflammatory fibrosis. The intima is no longer smooth, permitting the light yellow media to shine through; the patches of aortitis are whitish in color. This process begins about one centimeter above the aortic ring, and is usually most marked in the ascending portion of the aorta, though it frequently involves the entire thoracic aorta. Occasionally the whitish plaques and wrinkling are found in the abdominal aorta, even as far as the division into the common iliacs. The process may be quite marked about the mouths of the main vessels arising from the arch and the intercostal arteries, but it rarely extends along the course of these vessels.

Histologically, the process is characterized particularly by the presence of perivascular infiltration of the vasa vasorum, which begins in the adventitia but develops also in the media, and by the new formation of capillaries extending into the media. Later, perivascular areas of connective tissue with round cells and plasma cells may be found, and scar formation within the media, the retraction of which is responsible for the wrinkling and furrowing of the intima. The perivascular inflammation and formation of new capillaries are of most importance in the diagnosis. In the series studied, the anatomical diagnosis, if in any way questionable, was confirmed by microscopic examination. In the last five months of the year, after this study was planned, the diagnosis was not made by the pathologist, Dr. Jaffe, or his assistants unless confirmed microscopically.

The differentiation must be made from loss of elasticity, atheromatosis and aortitis of nonspecific origin. Simple loss of elasticity is characterized by fine wrinkling, longitudinal and parallel as compared to the coarser wrinkling with the marked irregularity of syphi-

lis. The presence of atheromatosis is characterized by plaques, hyaline and fatty atheromatous ulcers, and calcification. Fatty plaques, ulceration, and calcification are not a part of syphilis alone. Atheromatosis is a simple degenerative process, unassociated with inflammatory changes in the adventitia or media. There may be degeneration of the media without newly formed capillaries or cellular infiltration. The ultimate decision is with the microscope. In younger individuals the picture of syphilitic aortitis is usually clear; the intima has lost its smoothness, shows irregular wrinkling and puckering and the color changes from light yellow to white. In older individuals the presence of atheromatosis clouds the picture and makes microscopical examination imperative for diagnosis. The frequent coincidence of aortic syphilis and atheromatosis is responsible for the difficulties encountered in the attempt to estimate the clinical significance of either process.

The differentiation of syphilitic aortitis from rheumatic or nonspecific aortitis is difficult; in both conditions the perivascular infiltration is found, but in the rheumatic type this is more strictly confined to the adventitia and probably does not invade the media beyond its outer third, that part of the media adjacent to the adventitia. The diagnosis, however, rests largely upon the history and stigmata of syphilis in one group, the history and presence of other signs of rheumatic cardiac disease in the other. It is very difficult to differentiate the etiology of perivascular scars.

One hundred and nineteen autopsy reports were studied. In 19 instances the weight of the heart was less than 300 grams. Forty-four of the hearts weighed between 300 and 450 grams, and 51 over 450. In 5 instances the exact weight of the heart was not recorded. The largest heart weighed 1,060 grams. This was from the body of a man sixty-six years old. Another heart weighed 1,000 grams, and 8 weighed over 700 grams each. The myocardium presented no characteristic findings. Twice fresh infarctions were found and six times old scars, probably of vascular origin. One of these had resulted in a cardiac aneurysm and another had caused the replacement of about the upper one-third of the ventricular septum with a fibrous scar. Parenchymatous degeneration was described 14 times; in 10 instances this was associated with some severe infectious disease; once with carcinoma; once with atrophic cirrhosis; once with primary contracted kidney, and once with marked coronary sclerosis associated with primary contracted kidney. Cloudy swelling was described four times, twice with generalized tuberculosis.

In 4 instances there was partial obstruction of one of the larger branches of the coronary circulation; once an occlusion was complete. In 49 instances it was noted that the coronary vessels were narrowed or contained numerous plaques. The coincident occurrence of gener-

alized arteriosclerosis with the syphilitic changes in many of these cases makes it impossible to separate the two factors in the consideration of coronary disease. In 10 instances, however, the reports justify the conclusion that the typical wrinkling of syphilitic disease had involved the aortic intima about the coronary orifices. These figures are somewhat less than Dr. Jaffe anticipated. One striking statement is found in the report of an autopsy upon the body of a woman of twenty-four years. "Orifices are narrowed with wrinkling about them."

The cardiac hypertrophy as shown by the weight of the heart may be further illustrated by the measurements of the ventricles. Kaufmann quotes Krause as authority for the statement that the normal thickness of the right ventricle is from 5 to 7 millimeters; that of the left from 11 to 14. In this series, the thickness of the left ventricle was more than 14 millimeters (the maximum normal just quoted) in 87 instances; in 61 of these, this measurement was more than 18 millimeters; of 38 hearts in which the thickness of the left ventricle was more than 20 millimeters, 28 weighed more than 450 grams. In this same group aortic insufficiency was diagnosed anatomically 12 times, primary contracted kidney 6 times, secondary contracted kidney twice, and eccentric hypertrophy with benign arteriosclerosis of the kidney 5 times. (This last term as used in the pathological report appears to be most closely related to the condition regarded clinically as hypertensive heart disease.) In the whole series the thickness of the right ventricle was more than 7 millimeters, only 10 times; in all of these the left ventricle gave measurements above the maximum cited, although in one case in which death had resulted from chronic pulmonary tuberculosis, the left ventricle was only 15 millimeters thick; of the other 9, 5 were cases in which the total cardiac weight was over 600 grams. In one instance death was the result of malignant endocarditis of the pulmonary valves, in another of mesothelioma of the pleura. Of the 10 cases of right ventricular hypertrophy, one-half were a part of an extreme cardiac enlargement, and 3 were the result of a chronic disturbance of the pulmonary circulation.

In a number of instances small pericardial effusions were noted. In 19 cases more than 100 c.c. of fluid was found. In 8 of these there was decompensation with general anasarca; the amounts of fluid found varied from 100 c.c. to 300 c.c. Four times the cause of death was uremia, due to contracted kidney, and once, uremia resulting from ascending infection of the urinary tract. In one of these five, and in another case of contracted kidney where the pericardial effusion was small, fibrinous pericarditis was present. Twice, serous effusions were found with aneurysm; once a hemorrhagic effusion following rupture of an aneurysm into the pericardial sac. Once bronchopneumonia was the cause of death, once mesothelioma of the pleura, and in another

case in which the largest effusion was found, 700 c.c. of the purulent fluid, a malignant endocarditis of the pulmonic valves was present. From the standpoint of gross pathology, syphilis is, at least, an infrequent cause of pericardial disease.

TABLE I

Cases 119.	
Weighing less than 300 grams	19
Weighing between 300 and 450 grams	44
Weighing more than 450 grams	51
Myocardium (no characteristic findings)	
Fresh infarctions	2
Old scars	6
Parenchymatous degeneration	14
(Associated with severe infection, 10)	
Partial coronary occlusion	4
Complete coronary occlusion	1
Coronary vessels narrowed or showing numerous plaques	49
Syphilitic wrinkling involving coronary orifices	10
Pericardial effusion (more than 100 c.c.)	19
(All attributable to some intercurrent disease)	
Aortic aneurysm	13
(Involving heart, 2)	
Aortic regurgitation	24

Aortic aneurysm was present 13 times; only twice was the heart involved. Once a small aneurysm ruptured into the pericardial sac. Once there was found an aneurysmal outpouching of a sinus of Valsalva. All of the aneurysms occurred in male subjects.

The diagnosis of aortic regurgitation was based on anatomical findings, not on the water test. The criteria were thickening, adhesion, and shortening of the commissures and thickening of the free edges of the leaflets with retraction. In one case of aortic insufficiency, marked dilatation of the aortic ring was noted. The anatomical diagnosis of aortic insufficiency was made twenty-four times.

From another point of view, these findings fall rather easily into the three groups already mentioned. In the first group, including those with hearts less than 300 grams in weight, there were 19 cases; of these, 18 died of some intercurrent disease. Under this term are included all cases in which death was due to some cause other than cardiovascular disease. Two presented anatomically the findings of aortic regurgitation; one of these had presented the clinical findings of cardiac disease; the other died of bilateral renal suppuration. While reference was made to systolic murmurs in some instances the clinical records indicate that in the 18 cases serious thought of cardiac disease had not been entertained. In 2 of the 19 cases the blood pressure had been over 160. Ten of the group were females. This might be expected in a group based on the small weight of the heart. The average age at death in this group was 47.9. Marked coronary sclerosis was found 5 times.

The second group includes hearts weighing between 300 and 450 grams (not more than 50 per cent above the commonly accepted normal); there were 44 of these. In 21 cases death was the result of some intercurrent disease; in 6 of these, cardiac disease had been recognized

TABLE II

	TOTAL	AVERAGE AGE	DEATH FROM INTERCURRENT DISEASE	BLOOD PRESSURE OVER 160	ANEURYSM	AORTIC INSUFFICIENCY	MARKED CORONARY SCLEROSIS
Group 1. Weighing less than 300 grams	19	47.9	18	2	0	2	5
Group 2. 300-450 grams	44	50.0	21	9	8	3	8
Group 3. More than 450 grams	51	48.0	8	28	5	19	18

clinically. In this group there were 8 aneurysms and 3 cases of aortic regurgitation. In 9 cases (20.4 per cent) the blood pressure had been 160 mm. or above.

In this group, primary contracted kidney was found once; apparently 3 cases diagnosed anatomically as renal arteriosclerosis with eccentric hypertrophy of the heart had been regarded clinically as hypertensive cardiac disease. In 8 instances marked coronary sclerosis was noted; in one of these there was partial occlusion of one coronary orifice. The record of this case contains this statement, "distinct wrinkling, especially about the coronary orifices." In this group the average age was fifty years.

In the third group, including hearts of more than 450 grams in weight, there were 51 cases; the average age was forty-eight years. In 8 cases, death was due to intercurrent disease; in 3 of these the presence of cardiac disease had been diagnosed. Aneurysm was present 5 times. Aortic regurgitation was found anatomically in 19.

The percentage incidence of aortic regurgitation was 37.2, as against 11.4 in the second group and 10.5 in the first. In 13 instances, the clinical records of those with aortic regurgitation had shown the blood pressure above 160. In 28 of the entire group the pressure had been over 160, a percentage incidence of 57.1 as against 20.4 already cited for the second group and 11.7 for the first group. Primary contracted kidney was present 6 times. Marked coronary sclerosis was noted 18 times; in 3 instances there was partial, and in one, complete closure of a main branch of the coronary circulation.

CONCLUSIONS

1. Except for the predominant left ventricular hypertrophy which resembles that of essential hypertension, the gross myocardial changes associated with syphilitic aortitis are not characteristic.

2. The incidence of myocardial degeneration as a result of syphilitic involvement of the coronary circuit is not great. The frequent occurrence of arteriosclerosis with syphilitic disease makes it difficult to separate these two factors as causes of coronary disease. Probably less than 10 per cent of the cases with aortic syphilis are associated with coronary disease of syphilitic character. In this series, a description of the involvement of the coronary orifices in the typical wrinkling of syphilitic aortitis was found only 10 times, an incidence of 8.4 per cent.

3. Aortic insufficiency is found in about 20 per cent of the hearts associated with syphilitic aortitis. It is the lesion most easily recognized and is most likely to be present in the advanced cases. In this series, it occurred in 19, or 37.2 per cent, of the hearts weighing over 450 grams.

4. Hypertrophy of the heart is a significant index of the degree of cardiac involvement in cardiovascular syphilis. This sign is absent in the latent stage of the disease but becomes increasingly important as signs of cardiac disease appear. In a group of 44 cases in which autopsy showed definite cardiac enlargement of various degrees, up to a maximum of 50 per cent, 21 died of intercurrent disease, and 15 of these had not been diagnosed as subjects of cardiac disease. Some of these presented symptoms of acute disease so marked as to cloud the picture, but others did not. Both aortic regurgitation and hypertension were infrequent in this group. The presence of an unexplained or "idiopathic" cardiac hypertrophy in individuals of middle life may well excite the suspicion of syphilis.

5. The two important causes of cardiac hypertrophy are aortic regurgitation and hypertenson, which latter is a common occurrence in this type of case. There is a significant incidence of contracted kidney with advanced stages of cardiovascular syphilis.

6. In this series, aneurysm was found more frequently in the cases characterized by relatively minor cardiac symptoms. These results seem to illustrate the frequency with which aneurysm may be present without involving the heart or causing symptoms of cardiac disease.

In conclusion, I wish to make grateful acknowledgment of my indebtedness to Dr. R. H. Jaffe, pathologist of the County Hospital, for helpful suggestions and criticism in the preparation of this paper.

DISCUSSION

Dr. J. W. McMeans, Pittsburgh, Pa.—It is my impression that many of the changes suffered by the heart in syphilis are indirectly attributable to luetic aortic

intimitis involving the coronary orifices and leading to partial or complete occlusion of these vessels.

Dr. George Herrmann, New Orleans, La.—We are interested in cases of hypertrophy in syphilitic heart disease with and without regurgitation. Dr. Carr spoke of the greater thickness of left ventricular wall as indicating preponderating hypertrophy. I would like to know whether any actual weights of the separated left and right ventricles were recorded so that the relative proportions of the left and right heart could be reported. I believe that such and only such figures are adequate. In a small series of some twenty-five syphilitic aortic regurgitation hearts I found relatively little real left ventricular preponderance.

Dr. H. E. B. Pardee, New York, N. Y.—I would like to know if you found any hypertrophied hearts which did not also have an aortic insufficiency or hypertension?

Dr. Carr (closing).—I think there were a number of cases moderately enlarged without regurgitation or hypertension. I hope to work up the data on this subject as part of a more complete study.

MICROSCOPIC PATHOLOGY OF CARDIAC SYPHILIS

CHAUNCEY C. MAHER, M.D.
CHICAGO, ILL.

IN SPITE of the fact that an immense amount of study has been devoted to the microscopy of cardiac syphilis, apparently there remains considerable dissension among observers as to that which constitutes the exact picture of this disease. May I preface the discussion of this subject by briefly stating our conception of the pathogenesis of cardiac syphilis and mention a few of the difficulties encountered in this type of study?

It is assumed that early in the second stage of a syphilitic infection a spirochetemia occurs in which the heart suffers early changes, reaching the major involvement when aortic regurgitation supervenes. The pathological picture present varies with the amount and efficacy of treatment, with the resistance developed in the individual, and probably with the malignancy of the strain. Pathological entities other than syphilis, such as hypertension, arteriosclerosis, and other chronic or acute infections, may distort the picture. Terminal death-producing phenomena merit a special mention. From another standpoint it would seem exceedingly important to mention that syphilis is particularly likely to be localized in its activity. It is for this reason that I would like to present to you the following method of selection of material to disclose adequately the true microscopic picture of cardiac syphilis. Sections to be studied were chosen from the following:

Aorta, one inch above the valves.
Aorta, two and one-half inches above the valves.
Aorta, mid arch.
Aorta, descending portion.
One block through commissure of aortic valves.
Six to ten blocks of the larger coronary vessels.
Two blocks from the upper part of the septum.
One block from midseptum.
One block from lower septum.
Three blocks from each of the right and left ventricular walls.
One block from the right and left auricular muscle.
One block from the papillary muscle.
Blocks were also taken from any particular spot where any gross muscular pathologic change was evident.

The cases selected for study are necessarily limited, because of the previously mentioned distorting factors. Inasmuch as aortic regurgitation represents the acme of syphilitic involvement of the heart, both as to the extent and severity of the process, only this entity was chosen.

Furthermore, cases in which hypertension, renal disease, acute and chronic infections, arteriosclerosis and those in which death was a lingering process were excluded, leaving syphilis as the single lethal factor.

There are essentially three modes of attack for study of this problem. One may study the inflammatory cellular reaction, with its subsequent replacement by connective tissue, or the degenerative changes which the parenchyma undergoes, or finally, that which is probably the most difficult, staining the spirochetes *in situ*. Obviously, it is

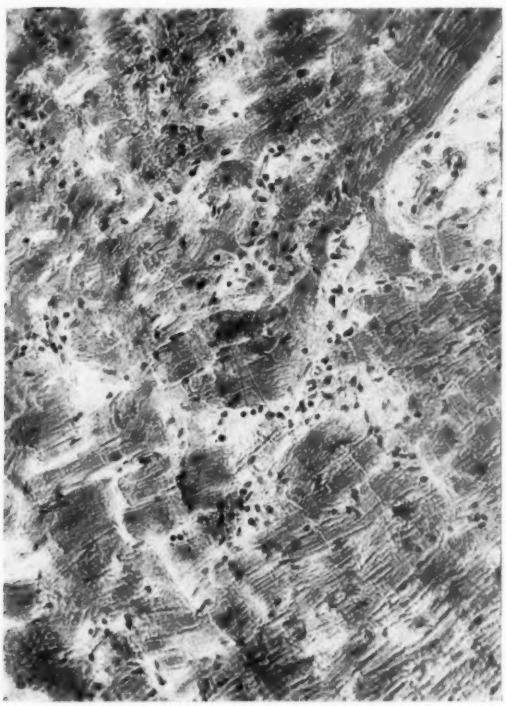

Fig. 1.

upon this latter method that the whole question revolves. A simple method for the demonstration of spirochetes, workable in all hands, is a necessity. Adaptations of the neuropathologist's staining methods for inflammatory cellular reactions will undoubtedly add much to our knowledge. The scope of this preliminary study is limited to the demonstration of the cellular infiltration, with reference to its location and extent by the ordinary hematoxylin-eosin stain.

The general pathologist and the neuropathologist have stressed the presence of lymphocytes, plasma cells, new connective tissue elements, and the endothelial proliferation in the blood-vessel intima, with new blood-vessel formation as criteria of active syphilitic involvement. The

cellular infiltration about blood vessels is generally accepted. I would like to point out the similarity of the microscopic picture of general paresis and that of aortic regurgitation, stressing the vascular phenomena, the visceral pericardial changes and the muscular infiltration.

Coronary Arteries.—The main arteries and their larger branches are the seat of a round-cell infiltration which is exactly like that seen in the aorta. In the first few centimeters of their courses this is liable to be exceedingly dense. As the arteries subdivide, the collections of cells become less frequent and smaller in size. The invasion is characteristically located in the adventitial coat but may invade the media or

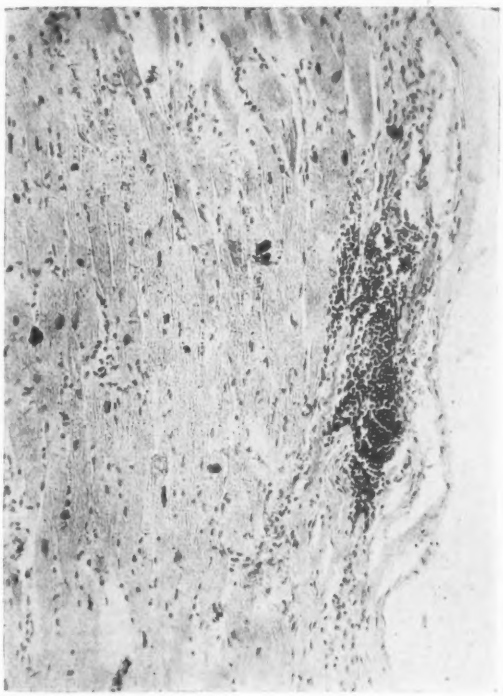

Fig. 2.

the subintima. In addition to the acute process, connective tissue replacement may be seen, particularly in the media. In the larger vessels intimal proliferation with subsequent hyalinization, while apparently a part of the syphilitic process in these cases, has also been observed in other types of disease.

Visceral Pericardium.—Localized groups of lymphocytes and plasma cells were commonly encountered in the visceral pericardial membrane and beneath it. A more common finding is a more scattered infiltration of these same cells. Apparently the end-result here is the same as in any syphilitic process, i.e., connective tissue proliferation with thickening of the visceral pericardial layer. Dr. Jaffe, chief of the

pathology department of Cook County Hospital, to whom I am indebted for his efficient criticism of this work, informs me that these larger areas may be detected grossly.

Myocardium.—In the septum and in the walls of either ventricle this same infiltrative process may be seen. It was seldom found as a diffuse uniform process. Some sections were without findings; others showed localized areas of infiltration with apparently normal muscle intervening. In the interstitial tissue when a vessel is cut in cross-section, one commonly finds a scattering of lymphocytes and plasma

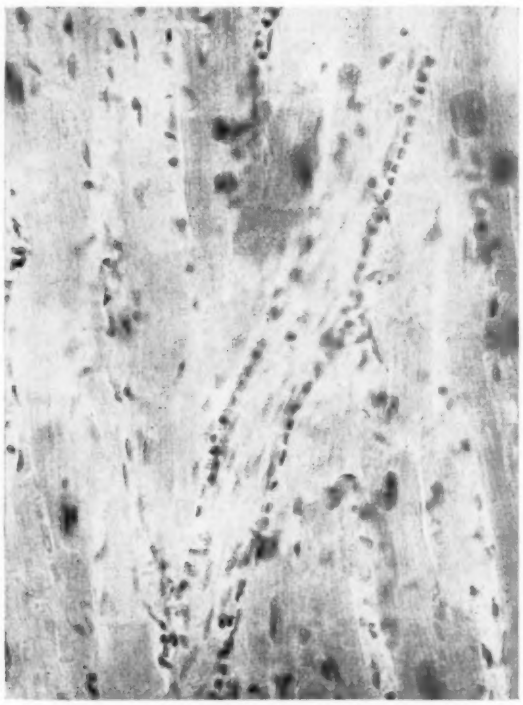

Fig. 3.

cells in the loose fibrillae. Sections showing the muscle fibers longitudinally with the interlying capillary frequently have a single layer of round cells lying about it. This single-file arrangement of cells between the muscle fibers was pointed out by Warthin some years ago. Patches of fibrosis composed of connective tissue of varying age are quite common.

Fig. 1 shows a diffuse round-cell infiltration in the muscle taken from the wall of the left ventricle. Fig. 2 shows a localized group of round cells near the epicardium extending into the muscle. Fig. 3 shows a capillary cut tangentially with the endothelial elements appearing dimly out of focus, with a single layer of round cells lying just

outside the wall. This latter is a characteristic picture but not readily demonstrable.

SUMMARY

Five cases of uncomplicated and probably untreated aortic regurgitation were studied microscopically from many sections. A method of selection of blocks of tissue for intensive study is presented. The inflammatory reaction, presumably due to syphilis, by exclusion of other factors was found to be a lymphocytic and plasma cell infiltration about the coronary arteries and their branches and beneath the visceral pericardium. In the muscular tissue the invasion appeared between the fibers and can be demonstrated about the capillary walls.

DISCUSSION

Dr. E. P. Carter, Baltimore, Md.—We have been interested in this question of differentiation of the luetic process, and we have noticed particularly these areas of diffuse, round-celled infiltration, but we have no positive proof that it is the syphilitic process. Does Dr. Maher feel that he can make a diagnosis from his findings in the absence of a history of syphilis? Another question, why does the lesser circulation seem to remain so constantly free from any syphilitic involvement?

Dr. Kurtz, Madison, Wis.—How often was this infiltration found? Was it found in 100 per cent of cases? Was there any difference noted in cases with aortic aneurysm and those with aortitis higher up?

Dr. Paullin, Atlanta, Ga.—I would like to ask if the speaker has demonstrated spirochetes in the pericardial lesions.

Dr. R. W. Scott, Cleveland, Ohio.—Had you any criteria to differentiate the myocardial lesions in coronary disease from those seen in diseased hearts from other causes?

Dr. Maher (answering Dr. Carter).—I do not think I would be able to make this diagnosis without the clinical history. I do not know why the smaller vessels remain free. In regard to aneurysm and regurgitation, we studied few aneurysms intensively, but aneurysm affects the heart itself least, regurgitation most, and aortitis lies between. I have never demonstrated spirochetes, but I think they are there. I have used Dieterle's and Warthin's stain, also Levaditi's stain. Answering Dr. Scott, the coronary artery picture is the same in syphilitic lesions as in lesions from other causes. The vessels show round-cell infiltration.

Dr. W. W. Hamburger, Chicago, Ill.—Does Dr. Maher feel that this picture of microscopic pathology should be taken as evidence of active untreated syphilis, or had these patients been treated?

Dr. Maher.—These were untreated cases. The people were not of the intelligent class, just the type that come to a dispensary clinic. In one case that received arsphenamine, there was no difference in the picture of round-cell infiltration.

THE LOCALIZATION OF THE LUETIC VIRUS IN THE AORTA

J. W. McMeans, M.D.
Pittsburgh, Pa.

SYPHILITIC aortitis is insidious in its onset and is, as a rule, chronic and progressive. Primarily it is considered to be a granulomatous inflammation of the periarterial tissues and adventitia characterized by lymphatic and perivascular lymphocytic infiltration and endothelial-cell proliferation. The intimal endothelium of the arterioles proliferates and in many instances leads to occlusion of the vessels. In places miliary gummata are formed. From the adventitia the syphilitic granulomatous reaction progresses by contiguity to involve the other tissues of the aortic wall.

In 1927 Peck[1] reviewed the literature on syphilis of the pulmonary artery and reported one case of this disease. He remarked that the necrotic gummatous formations of the severest type may remain entirely localized to the intima of the pulmonary artery and states that this is contrary to the observations so far described in the pathological anatomy of gummatous aortitis in that, in the latter, there is a total syphilitic mesaortitis. In the same year Saphir and Cooper[2] described a case of acute suppurative aortitis superimposed on syphilitic aortitis. They stated that the whole intima presented an increase in connective tissue and areas of hyalinization, in some of which a few endothelial cells and plasma cells were found. In addition to these changes, large formed vessels extended up to the intima and were surrounded by lymphocytes and circumscribed areas of leucocytic infiltration. They noted that the acute suppurative aortitis was formed exclusively in the intima and inner portion of the media, which areas are supplied not by the vasa vasorum but by the circulating blood. A diplococcus lanceolatus was recovered from the blood at autopsy.

In the past several years I have had an opportunity to perform necropsies in the service of Dr. W. J. McGregor, coroner of Allegheny County, Pennsylvania, and I have been fortunate to find a large number of cases of syphilis of the aorta in its various stages.

One of the outstanding features of this disease is the capillary endothelial-cell proliferation which it is agreed constitutes a typical obliterating endarteritis. For some reason or other a peculiar chemotactic influence is exerted upon endothelial cells of lymph spaces and capillaries by the virus of syphilis. If this is true in the case of the vasa vasorum of the aorta and again in the intima of the pulmonary artery, there is no reason why endothelium in other locations should not respond to the influence of the virus. Certainly, the endothelium of the

aortic intima differs in no material way from those already mentioned, and there is some evidence to show that there is a reaction in aortic intima which is comparable to that which is considered characteristic for syphilis in the outer coats of this vessel.

That the syphilitic granulomatous reaction does not remain limited to any part of the wall of the aorta is illustrated by the findings in a case of an individual (W. B. W., Nov. 14 1929) found dead in a rooming house. No history could be obtained. Grossly the wall of the aorta was thick and tough. The intima was wrinkled and puckered. The condition involved the base of the vessel extending into the sinuses of Valsalva. The aortic leaflets were moderately shrunken. The mitral valve was healthy. The coronary orifices were pin-point in char-

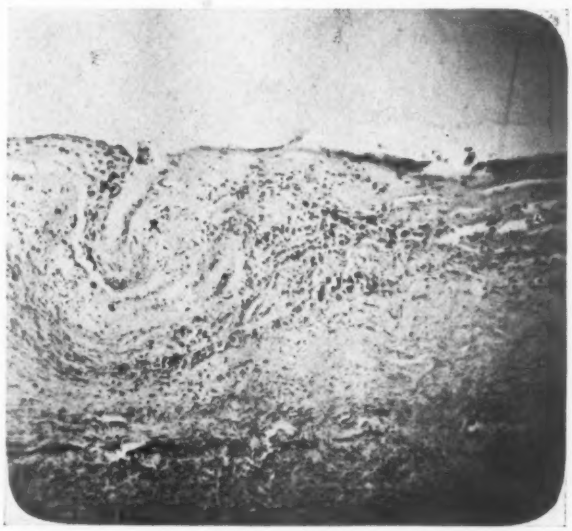

Fig. 1.—Low power field showing older crevice-like lesion in intima (W. B. W.) with surrounding inflammatory reaction.

acter and surrounded by thickened pinched-in intima. The greater part of the aorta was involved with the condition extending into the lower part of the abdominal portion.

Microscopically a section of the aorta through the orifice of the left coronary artery showed a thick, pink-stained, laminated intima in the lower layers of which there were cells with large, swollen, stippled nuclei. Just beneath this region there were the outposts of lymphocytic infiltration. These cells were related to a rich nest of capillaries that were situated just beyond the first cellular layers of the intima. The larger cells were endothelial in type and situated in the perivascular lymph spaces about these vessels. Red blood cells were present in all of these vessels. The vessels were centered in a matrix of cells which had swollen, oval, round or spindle-shaped nuclei. Caught in

the interstices of this meshwork there were lymphocytes and occasional polynuclear leucocytes. Capillaries and a typical granulomatous inflammation were followed through the wall at irregular intervals from the adventitia.

A section of the left coronary artery at its origin showed a proliferation of the intimal endothelial cells in a fine papillary arrangement with the cells at right angles to the surface. Numerous leucocytes and occasional lymphocytes infiltrated the intima and extended for a short distance into the wall. There was no evidence of atherosclerosis. The reaction in the intima of the aorta and in the intima of the left coronary artery were contiguous and presented all the characters of a typical syphilitic granuloma. Such areas of intimal change are prone to

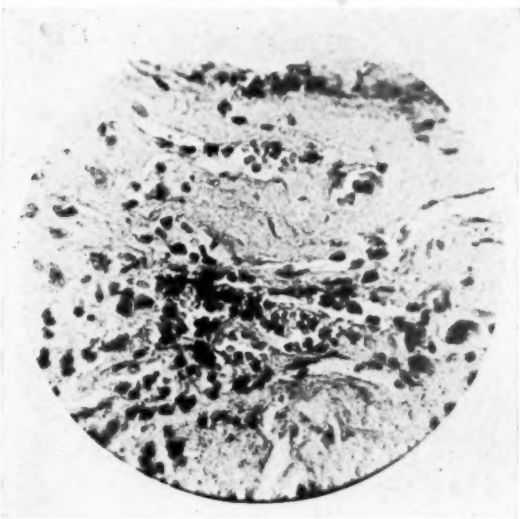

Fig. 2.—High power field of case (W. B. W.) showing endothelial cell proliferation and vascularization of deep intimal tissues. About orifice of left coronary artery.

undergo necrosis with the development of an ulcerative intimitis which may serve as a focus for the entrance of an acute mycotic invasion of the wall or of itself foster the formation of a mural thrombus. Over such areas of granulomatous change I have observed the margination of leucocytes upon the intimal endothelium and then the penetration of the leucocytes into the subjacent superficial layers, internal to the remnants of the frayed and hypertrophied internal elastic layer. In review, the cause of death in this case was coronary occlusion secondary to a luetic intimitis of the aorta.

Recently I have observed three cases of mural thrombosis of the ascending aorta complicating ulcerative luetic intimitis not associated with fatty degeneration or atheromatous change in the intima. In all of these cases the aortic and mitral valves were healthy. In the first

case (M. W., Sept. 16, 1929) the intima of the ascending aorta was smooth and pale. As the arch was reached, the intima changed in character, becoming finely wrinkled and puckered. The intima of the branches of the arch showed a similar appearance at their orifices. Here the wall of the vessel was from two to three times as thick as in the ascending or thoracic parts. On the posterior wall there were three firmly adherent, grayish-red thrombi, one of which measured 1 cm. in diameter. The latter clot was situated just below the orifice of the innominate artery. The other two clots were pea sized.

A section of the aorta showed a marked perivascular infiltration of lymphocytes about the vasa vasorum. Associated with the lympho-

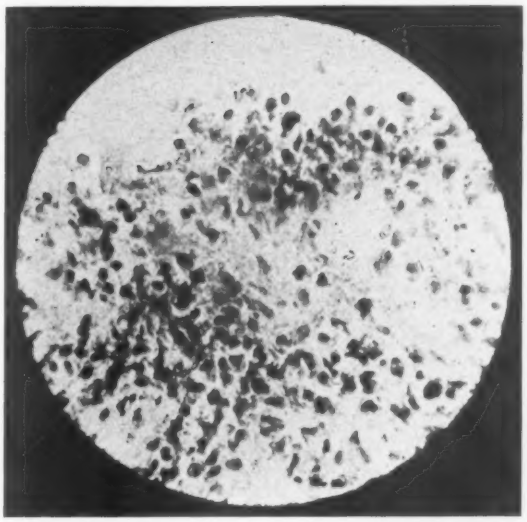

Fig. 3.—High power field from another case (H. W.) showing suggestive papillary arrangement of intimal reaction about orifice of left coronary artery.

cytes there were numerous plasma cells and some endothelial cells. These small arterioles were surrounded by thick whirls of connective tissue, and their lumina were irregular in outline. The outer coats of the small vessels were infiltrated by the inflammatory cells. In the intima overlying this reaction there was a loose vascular meshwork, the vessels of which contained red blood cells. About these vessels there was pink-stained, fibrillar tissue in which occasional elongated nuclei were seen. Lymphocytes and plasma cells together with occasional large mononuclear cells which had single large nuclei and irregularly shaped pyramidal cell bodies infiltrated the tissue. Numbers of cells were seen which showed two nuclei. This inflammatory zone led to a hillock where the thickness was entirely limited to the intimal tissues. The lower border of the elastic layer could be followed along

beneath this raised area. Over the surface of the raised area there was a single layer of flattened endothelium. Between this endothelial covering and the internal elastic layer there was a striated network of

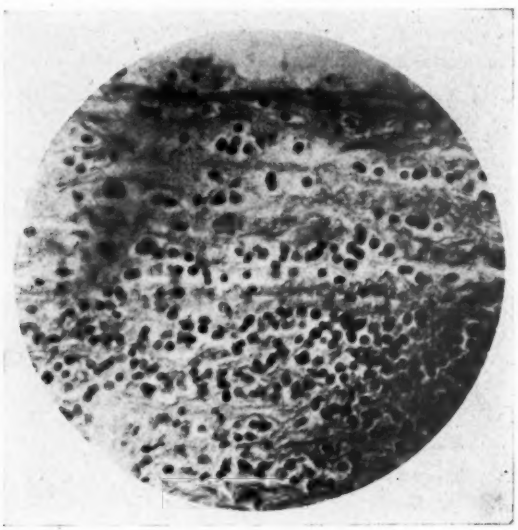

Fig. 4.—High power from field from border of intimal thrombus showing intimal reaction in case (M. W.). Note the endothelial cell proliferation with lymphocytes and plasma cell infiltration. There is débris upon the intimal surface.

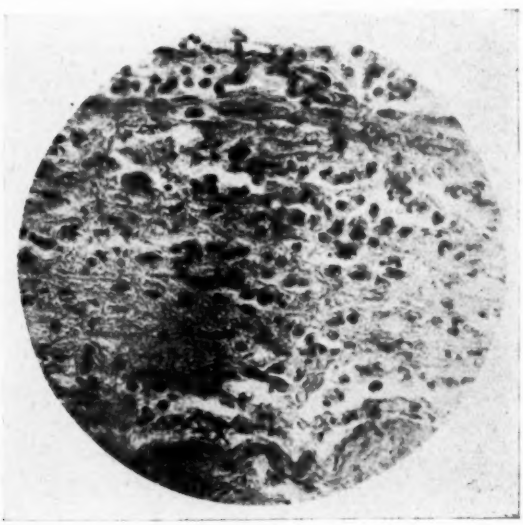

Fig. 5.—High power field of another area in intima of case (M. W).

pink-stained, fine fibrils in which there was incorporated homogeneous, pink-stained material. There were swollen, round and oval nuclei which stained moderately blue. In other areas they were just visible,

and about them there were pink-stained areas with the suggestion of indefinitely defined cell bodies.

Beneath this area in the media approaching the zone between the middle and inner thirds there were small blood vessels with perivascular infiltration which was like that found in the adventitia. Other areas of intimal reaction were seen where the tissue between the internal elastic layer and the endothelium was packed with lymphocytes and occasional polynuclear leucocytes. The numbers of lymphocytes gave the appearance of a chronic inflammatory reaction like a granuloma. As the intimal reaction was followed the numbers of lymphocytes increased to the edge of the thrombus which has been described in the gross specimen. This thrombus was laminated. It consisted of

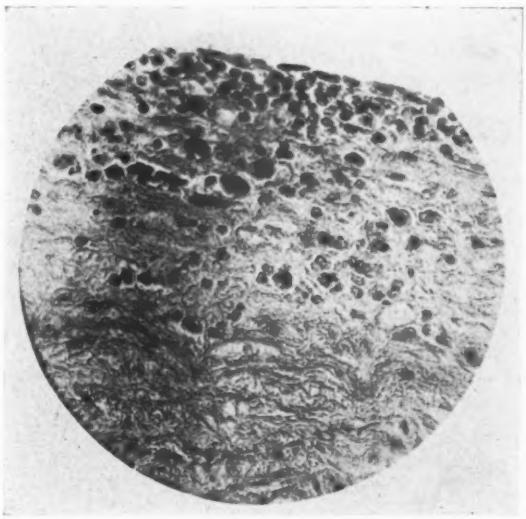

Fig. 6.—High power field showing intimal reaction in case (M. W.). Note the large multinucleated cells and endothelial proliferation.

pink-stained fibrillar material and concentrated pink-stained clumps. The character of the inflammatory reaction associated with this clot was not of an acute nature. Leucocytes were not found in it. Large numbers of swollen, round, oval and elongated spindle-shaped cells were seen invading a finely reticulated pulp. The reaction was entirely between the elastic layer and a thin zone of lymphocytes which covered the ulcerating surface. In another area the reaction dipped through the internal elastic layer. Lymphocytes and swollen mononuclear cells and fibroblasts were seen in the area. A wedge-shaped extension followed through the internal elastic layer to a small blood vessel which was almost at the inner border of the media. Below this there was a network of vessels in the media and adventitia. In another area there was a layer of blood clot, part of which was infiltrated by

leucocytes. Part of the clot was necrotic. In some places free blood still remained in the clot. Some large mononuclear cells with swollen nuclei were seen. On either side of the thrombus flattened endothelial cells were found extending over the surface. In review, the cause of death in this case was acute alcoholic gastroenteritis. The findings in the aorta were incidental, and they constituted an early but well-defined syphilitic intimitis which had undergone gummatous necrosis. The vital first part of the aortic intima was uninvolved.

In the second case (F. Z., Oct. 31, 1929) at a distance of 2 cm. above the right anterior aortic segment there was a raised, firmly attached greyish-red thrombus which measured 2.5 × 1.5 cm. It extended almost entirely across the anterior face of the intima. From the lower end of the thrombus a tail of red granular clot extended into the left coronary artery almost completely occluding it. This part of the thrombus was not attached, and the intima of the coronary vessel was unaltered. The heart muscle showed no evidence of infarct. The aortic and mitral cusps were thin, smooth and glistening. The right coronary orifice and the intima of the sinuses of Valsalva were unaltered. The wall of the aorta was irregular, thick and tough, and the change persisted to the level of the diaphragm. There was a fine puckering of the intima, but the greater extent of this membrane was puffy and glassy. The orifices of the vessels of the arch were irregularly dilated and surrounded by a thick wrinkled intima.

Sections of the aorta showed a marked thickening of the adventitia and an associated perivascular lymphocytic infiltration. The endothelial cells in the capillaries were hyperplastic, leading to almost complete occlusion of two of the vessels. Some large nerve bundles were seen in lymphocytic inflammatory zones, but apparently there was no infiltration of their substance. Small vessels could be followed from the adventitia into the wall of the aorta until they advanced to the inner border of the media. Associated with this vascularization there was a lymphocytic and plasma cell infiltration. The media was split and frayed by the reaction. Areas of cellular connective tissue cut through the media along the line of vascularization. Patent vessels were still present in these scars. Where the capillary tufts advanced to the subintimal tissues, the inflammatory reaction extended through to the intimal surface upon which there were pink-stained necrotic débris and a large massive thrombus of fibrin, blood, leucocytes, mononuclear cells and some eosinophiles. At one place in the intima there was a necrotic zone with numerous leucocytes, some lymphocytes and nuclear débris. Leucocytes could be traced from this area outward into the media where they were found free and in the small capillaries. In places the leucocytes formed massive collections. Beneath the thrombus fibroblasts were arranged radially to the intima, advancing into the base of the adherent thrombus. In review, this case showed

an advanced gummatous necrosis of the aortic intima resulting in a luetic intimal ulceration above the orifice of the left coronary artery. A thrombus formed upon this ulcer which extended downward into the left coronary orifice occluding it. Death resulted from coronary occlusion.

In the third case (H. G., May 19, 1930) the aortic leaflets were free, smooth and glistening. Above the junction of the right and left anterior leaflets there was a grayish-red thrombus which extended across the face of the aorta 0.5 cm. above the left anterior leaflet, passing into the left coronary orifice, practically occluding it. The thrombus was attached. It measured 1.6 × 1 cm. and projected on the surface a distance of 0.3 cm. The thrombus extended into the coronary orifice a distance of 0.3 cm. The intima of this vessel was not puckered or wrinkled, and it did not show any areas of atherosclerosis. The intima about the orifice was mucoid, watery and edematous, and for a distance of 2 cm. above the upper level of the leaflets there were fine furrows. The orifice of the right coronary was slit-like and not larger than a pinhead. About it there was a thick, bluish-white, mucoid nodule. There was some puckering and wrinkling of the intima of the left anterior and of the posterior sinuses of Valsalva. The intima of the aorta beyond the zone of 2 cm. above the upper border of the aortic leaflets was pale yellowish-white. In the middle of the posterior wall of the left ventricle of the heart there was an almond-sized infarct which was undergoing coagulation necrosis. In the meshes of the infarct there was a coagulated material like gelatin. This infarct was associated with a change in the finer radicles of the right coronary artery. There was also a small red infarct in the anterior surface of the upper pole of the right kidney.

A section through the thrombus showed no macroscopical evidence of atheroma or calcification in the wall. The thrombus was situated upon a bluish-white, pearly, edematous nodule in the intima which measured 0.2 cm. thick. The entire thickness of the wall through this area was 0.5 cm. When the thrombus was included, the thickness was increased to 0.75 cm.

Microscopically a section of the aorta through the clot above the left coronary artery showed a pink-stained, clumpy material in which there were scattered leucocytes, lymphocytes, swollen endothelial cells and fibroblasts. There were some small irregularly defined spaces in which there were unevenly placed swollen endothelial cells. Red blood cells were found in these spaces. The thrombus rested upon a base of leucocytes, lymphocytes and endothelial cells. From this ulcer to the level of the internal elastic layer there was a laminated, pink-stained tissue in which thin, fibrillar, deeply stained nuclei were distributed. Leucocytes extended into this tissue for some distance. As the base of the ulcer was followed toward the orifice of the coronary artery,

numerous small cleft-like spaces were developed. These spaces were lined by endothelial cells that had oval and round nuclei. Some of them were deeply stained, others were vesicular. Many of the spaces were completely filled with these cells. Lymphocytes, some leucocytes, and occasional eosinophiles were seen in the tissue.

Below this zone there was a necrotic tissue which involved the intima and the media. Nuclear débris, blue-stained, granular material and leucocytes infiltrated this area. Gram-Weigert sections were negative for microorganisms. The leucocytic infiltration could be traced through to the midportion of the media where irregular areas of this layer were necrotic and infiltrated by leucocytes. The necrosis of the media stopped at the level of the large vasa vasorum. Numbers of

Fig. 7.—Low power field of case (H. W.) showing intimal reaction about orifice of left coronary artery.

large cells with irregularly shaped, bilobed granular nuclei were found in the region of these vessels. Leucocytes were present in this granulomatous area. They could be followed from the intima through the media to it. In the outer part of the media there was endothelial cell proliferation in the vasa vasorum and perivascular spaces with numbers of lymphocytes, some plasma cells but no leucocytes. There was no evidence of atherosclerosis.

At the border of the thrombus the intima was puffy and meshy in character. It had the microscopic appearance of what might represent the mucoid, bluish-white, intimal thickening noted macroscopically. The surface endothelial cells were swollen and hyperplastic. Beneath this layer there was a zone of 10 to 12 cells irregularly arranged in a loose reticulated tissue. These cells consisted of swollen, spindle-

shaped fibroblasts, with pale stippled nuclei, deeply stained round cells and some plasma cells and an occasional leucocyte. Here and there a small space was lined by hyperplastic endothelial cells with pale vesicular nuclei. This proliferation of cells continued down to the inner border of the media. In this section it appeared that the intimal reaction was independent of that found in the media in other places, as the media in these sections was free. In review, this case showed a gummatous necrosis of the aortic intima resulting in a luetic intimal ulceration upon which a thrombus formed. The thrombus extended down into the left coronary orifice occluding the vessel. Death resulted from coronary occlusion.

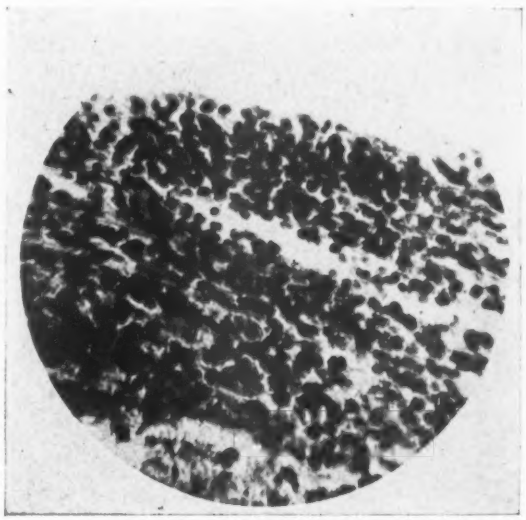

Fig. 8.—High power field showing a dense inflammatory intimal reaction (H.g.).

In these cases the zones below the thrombi on the intimal surface were packed with lymphocytes and leucocytes. Endothelial and fibroblastic hyperplasia was associated with small capillaries in the base of the thrombi. In the first case at the border of the thrombus endothelial cells were found extending up over the surface of it. These findings are indicative of advanced healing in this thrombus, and from this there is reason to believe that certain areas of intimal sclerosis may be healed thrombi rather than productive sclerosis secondary to deep intimal and inner medial change. If such is the case, we must remember the idea of Rokitansky[3] concerning intimal sclerosis, and yet the findings in these cases are not at variance with the views expressed by Virchow.[4]

All of these cases show massive destruction of areas in the aortic wall proceeding outward through the wall from areas of ulcerative luetic intimitis. Under conditions of ulceration like those observed in

these cases it is not at all improbable that extensive destruction of the wall of the aorta and even rupture of an aneurysm may be accounted for by the extension of a progressive gummatous inflammation from the intima of the vessel through the wall.

The manner in which the intimal ulceration occurs is problematical. In certain areas hyperplastic surface cells show granular cytoplasm with poorly stained nuclei and blurred cell outlines. In these places the zones between the intimal endothelium and internal elastic lamella are crowded with inflammatory cells. This would naturally lead to ulceration at the point of least resistance, which is upon the intima. When this occurs a raw surface, so to speak, is produced, upon which the elements of the blood may gravitate with resultant thrombus for-

Fig. 9.—Low power field showing thickening of intima with inflammatory infiltration (H.g.) Media is free.

mation. Some years ago I called attention to the intimitis which occurs in the vessels of the brain in meningitis and suggested that such a condition may precede thrombus formation.

Although blood cultures were not made in these cases, the possibility of mycotic invasion of the wall through areas of intimal ulceration cannot be discounted. Aside from the bacteriological findings the cases included in this report are not unlike the case reported by Saphir and Cooper. However, the findings in these cases suggest that the granulomatous intimal change precedes the advent of the acute inflammatory invasion of the intima. A gummatous necrotic area in the intima would form a favorable nidus for the localization of organisms circulating in the blood. However, the reactions observed in the aortic intima of these cases would indicate that gummatous necrosis is of

itself sufficient to be responsible for the entire changes noted. The attraction of leucocytes to such areas does not necessarily imply mycotic invasion. It is only necessary to mention the leucocytic infiltrations seen in the media of the aorta in gummatous necrosis of this layer and those leucocytes found in and about areas of infarcted heart muscle. The leucocytes respond to chemotactic influence of the necrotic process even in the very early stages of gummatous necrosis. This is clearly shown in the first case where margination of leucocytes upon an area of unbroken luetic intimitis had occurred. Furthermore, leucocytes could be traced for some distance into the underlying tissues. Although the secondary leucocytic reaction in this case was mild, it is possible that it represented the prestage of the more severe reactions described in the last three cases.

Although it is impossible definitely to indicate the final results in these cases, it would appear that there is some evidence to support the contention that nodular thickenings of the intima noted in syphilitic aortitis are not entirely due to secondary reactive fibrosis subsequent to medial damage. When the process is not too severe, rapid and extensive, the intima may recover and heal. We have seen that the inflammatory process in the intima is accompanied by progressive as well as by secondary acute degenerative changes.

Fibroblasts and endothelial cells were found proliferating in the intima associated with small capillaries, lymphocytes and leucocytes. Under ordinary circumstances in the end, even when ulceration occurs, the fibroblastic proliferation would bring about the repair of the injured layer, leaving the intima thickened, puckered and hyaline in appearance. I have noted intimal puckering microscopically in zones of luetic intimitis where the underlying media was entirely free from inflammation or scarring. When ulceration occurs, thrombus formation is stimulated. Organization of such thrombi increases the probability of intimal hyalinization. However, with the advent of ulceration, thrombus formation and possibly mycotic invasion of the area, extensive destruction of the wall may follow. I have seen crypt-like ulceration in the wall of the aorta with destruction of the intima and media and red blood cells infiltrating the last few strands of the adventitia.

Virchow demonstrated that the intima, like other nonvascular structures, may be the seat of inflammation, and that a proliferation of its own cells leads to the nodular masses on the surface. In syphilis we are dealing with an inflammatory process of long duration, and the nodular thickenings which occur in the aortic intima may be comparable to certain other inflammatory reactions of the intima which are always accompanied by a connective tissue disturbance of a proliferative kind. If this were not true in part, at least, it would be difficult

to account for the changes noted in the nodular thickenings about the coronary arteries in two of these cases. Furthermore, when one considers the endarteritic process observed in the vasa vasorum of syphilitic aortitis, it is difficult to understand why this same granulomatous process cannot involve the intima of the aorta with the end-result in both instances the same, hyalinization of the injured tissue.

Mesaortitis has been considered in the past the important lesion of syphilis of the aorta. First, because it was so obvious microscopically, and second, aneurysm, a very important end-result of aortitis, was supposed to occur after destruction of the media. This idea held despite the fact that aortic regurgitation associated with a syphilitic aortitis represents the most serious end-result of syphilis on the cardiovascular system. This lesion can only be produced by involvement of the aortic intima. The media does not come into this picture at all. Furthermore, the closure of the coronary orifices, also a lesion of great importance, is purely an intimal manifestation of lues. Therefore, as Warthin has suggested, the term syphilitic aortitis is much to be preferred to syphilitic mesaortitis, both from clinical and pathological grounds. Our purpose is to indicate four cases in which there was luetic intimitis associated with the changes commonly recognized in the adventitia and media.

In the cases under discussion, as indicated by the photomicrographs, it is obvious that there is a syphilitic inflammatory intimal lesion. Intimal lesions due to syphilis are well recognized in small vessels under the term endarteritis proliferans. Further, they are known to occur in the intima of the pulmonary artery and Winternitz[6] has stated that in congenital lues there is marked involvement of the intima with spirochetes predominating in this layer. By analogy there is abundant proof that luetic intimal disease is not a peculiar condition and occurs far more frequently than is generally believed. The intima of vessels is prone to show acute inflammatory reactions in other infections. Some years ago I demonstrated the acute intimal lesions noted in the cerebral vessels in acute meningitis due to a variety of microorganisms and also showed that these small arteries were invaded simultaneously by inflammatory cells from the intima and adventitia.

If these facts are true, what proof is there to show that an acute luetic lesion of the aortic intima does not occur? From the reactions observed in the cases under discussion, there is ample ground to believe that intimal luetic aortitis does occur and further that the aorta is simultaneously invaded from the intima and adventitia. The media is secondarily involved from both of these coats and suffers in extent depending upon the severity of the process in the intima on the one hand and the adventitia on the other.

CONCLUSIONS

It is our belief that in syphilitic aortitis the intima is involved primarily by direct infection from the blood stream. It may also be involved from the adventitia through the vasa vasorum. Histologically, the lesions are the same.

Undoubtedly, the most serious lesions produced by syphilis on the aorta and heart are the syphilitic aortic endocarditis with regurgitation and occlusion of the coronary orifices. This is intimal disease. Therefore, it would appear that luetic intimal disease of the aorta is more important clinically than is medial disease.

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OBSERVATIONS ON 107 CASES OF SYPHILITIC AORTIC INSUFFICIENCY, WITH SPECIAL REFERENCE TO THE AORTIC VALVE AREA, THE MYOCARDIUM, AND BRANCHES OF THE AORTA

O. Saphir, M.D., and R. W. Scott, M.D.
Cleveland, Ohio*

THIS paper presents in summary form the salient pathological features observed in 107 cases of syphilitic aortitis with involvement of the aortic valve area. A more detailed report of this work will be published shortly.

Gross Changes in the Aorta.—Characteristic gross syphilitic lesions were found at the aortic root, including the first 4 cm. of the vessel in all cases. These changes extended upward as far as the arch of the aorta in all but two instances. Gross syphilitic lesions in the descending aorta occurred in 20 cases. In 91 instances the descending aorta showed changes due to arteriosclerosis. In 26 cases a definite dilatation of the aortic ring was noted. Aneurysmal dilatation of the aorta was found in 16 instances, 3 in the first segment involving the sinus of Valsalva, 7 in the ascending arch, and 3 in the descending aorta. In two cases both the first segment and the ascending arch were involved, and in one both the ascending and descending aorta.

Histological Changes in the Aorta.—In addition to the well-known medial changes of syphilitic aortitis, we were impressed, particularly in early cases showing minimal gross lesions, by the frequency of involvement of the vasa vasorum in the adventitia. The vessel wall was thickened with more or less obliteration of the lumen. In early cases showing a lesion of the adventitial vessels, changes in the media were minimal and often difficult to demonstrate. This obliterative arteritis of the vasa vasorum of the adventitia with perivascular infiltration of lymphocytes was the most characteristic finding in both early and late cases.

Changes in the Aortic Valve.—All cases showed some grade of deformity in the architecture of the valve cusps. The commonest finding was a widening of the commissure. In 82 instances the commissures were the seat of hyaline plaques. The central portion of the free margins of the cusps was thickened in 82 cases, everted or rolled in 20, and retracted in 8.

Histological Changes.—Characteristic syphilitic lesions were found in all cases in sections from the region of the commissures and adjacent

*From the Departments of Pathology and Medicine of the Cleveland City Hospital and Western Reserve Medical School, Cleveland.

portions of the cusps. The new formation of smaller sized vessels extended from the aortic intima through the commissures to the lateral portions of the cusps in early cases. In older lesions the degenerative changes were less pronounced and those of chronic inflammation more evident. The central portions of the valve leaflet showed fibrosis and hyalinization, very few cellular elements and no blood vessels.

Coronary Arteries.—Thirty-seven cases, or 33 per cent, in this series showed some constriction of the mouths of the coronary arteries. In 8 the right coronary was narrowed; in 7 the left, and in 17 the mouths of both vessels were involved. Four cases showed complete obliteration of the left coronary, and one complete obliteration of the right. In four instances the coronary openings were definitely displaced. The histological changes at the coronary openings were similar to those observed in the aorta. The main stem and branches of the two coronaries were often the seat of simple arteriosclerosis, but in no instance were syphilitic lesions demonstrated in the coronary arteries themselves.

Other Large Arteries.—The innominate, carotid, superior and inferior mesenteric, iliac and femoral arteries were studied in 65 cases. Varying grades of arteriosclerotic changes were seen but no clean-cut gross lesions of syphilis were noted. Histologically, however, typical microscopic lesions of syphilis were observed as follows: Innominate artery in 38, carotid in 27, superior mesenteric in 12, inferior mesenteric in 3, common iliac in 11, and femoral artery in 7. In 44 cases the subclavian artery showed syphilitic changes microscopically in 19 instances.

Myocardium.—In 94 cases the heart weighed more than 400 grams. The heaviest heart in our series weighed 1050 grams. The average heart weight for the whole group of 107 cases was 600 grams. Frequently the cut section of the myocardium showed nothing unusual. In other hearts showing coronary arteriosclerosis the myocardium was the seat of fibrosis. In no instance did we find either gross or histological evidence to warrant the diagnosis of syphilitic involvement of the myocardium. The changes as noted differed in no way from those occurring in hearts hypertrophic from other causes, or in hearts the seat of coronary arteriosclerosis. Many sections were examined according to the Warthin-Starry method and also the Levaditi method, but in no instance was the spirocheta pallida found.

CONCLUSIONS

1. The primary and earliest lesion in syphilis of the aorta and larger arteries is an obliterative endarteritis of the vasa vasorum of the adventitia, with perivascular infiltration of lymphocytes. The medial changes appear to be secondary and attributable to nutritional disturbances.

2. The frequency with which syphilis attacks the root of the aorta is due to the rich supply of vasa vasorum in this region.

3. Syphilis spreads from the aorta to the aortic valves by way of small vessels at the commissure. The degenerative changes and later chronic inflammatory changes lead to fusion of the lateral margins of the leaflets with the adjacent aortic intima, producing a widening of the commissure; the most constant and characteristic gross lesion of syphilis of the leaflets. In no case have we seen a gross distortion of the aortic leaflet without involvement of the commissure.

4. Syphilis at the root of the aorta frequently involves the coronary openings, one out of three cases in this series showed varying degrees of occlusion, but no evidence of syphilis was found in the coronary vessels beyond the mouths.

5. Syphilitic involvement of large arteries—carotid, subclavian, innominate, mesenterics, iliac, and femoral arteries, is often found associated with syphilitic aortitis.

6. Invasion of the myocardium by syphilis is rare. The myocardial changes observed in this series of cases differed in no way from those seen in coronary arteriosclerosis and in hypertrophied hearts from other causes.

THE ROENTGENOLOGICAL DIAGNOSIS OF SYPHILITIC AORTITIS—A REVIEW OF FORTY PROVED CASES*

DAVID STEEL, M.D.
CLEVELAND, OHIO

THE data for this paper are taken from a study of forty cases of luetic aortitis observed roentgenologically and proved by autopsy. No case of aneurysm is included. The roentgen method varied somewhat but included in every case a fluoroscopic examination and teleroentgenograms taken for the most part in the postero-anterior position and in many cases also in both oblique positions.

It is needless to point out that the course of the aorta should be thoroughly understood in the various positions. The diagrams (Figs. 1, 2, 3) bring out the so-called normal silhouette in the average case, but there are in addition normal factors which play an important part in this configuration. These are concerned mainly with increased and decreased spacial relations of the thoracic cage. With a high position of the diaphragm (expiration, ascites, abdominal tumors, etc.) the cage is small and the aorta is spread, appearing more prominent to the right and left and increasing slightly in height. With low position of the diaphragm the vascular shadow is narrow, and bulging to the right or left is minimal. With foreshortening of the thoracic cage, as in caries of the spine, spreading again takes place. With advancing age the aorta elongates and in accommodating itself to spacial relations becomes spiral with an increase in its height.

In addition, the silhouette is not always sharply defined, anatomical relations are many times obscure, and the superior vena cava might add to, and the brilliant trachea subtract from, the apparent silhouette, especially in the first oblique view. Even with special care it is difficult to obtain plates in an exact postero-anterior view. These factors, combined with the spacial relations of the thorax, must all be evaluated as closely as possible. We therefore often have several factors present, the value of which is almost impossible to estimate and hence various proposed measurements have a decided limitation and can often lead to error. Nevertheless, if these limitations are recognized, measurements have a clinical value. Of the various methods, perhaps the simplest and most ingenious is that proposed by Kreuzfuchs; namely, measurement of the aortic width after barium visualization of the aortic bed of the esophagus. This method has been accurate at autopsy in the few cases I have proved. Unfortunately, the

*From the Roentgenological and Pathological Departments of the Cleveland City Hospital.

method measures the aorta near the isthmus rather than near the root where syphilis is more common and more important physiologically. Just as proficiency grows with experience in other fields of medicine,

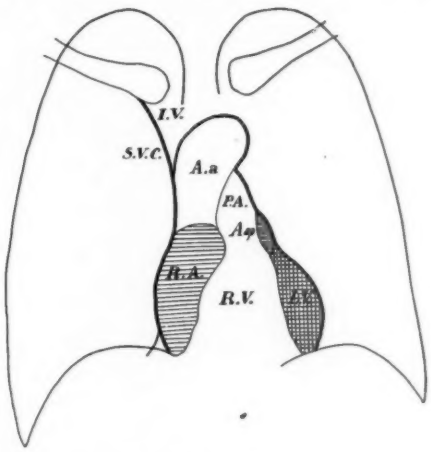

Fig. 1.—Diagram of the normal heart in the anteroposterior position. *S.V.C.*, Superior vena cava; *I.V.*, innominate vein; *A.a.*, ascending aorta; *P.A.*, pulmonary artery; *A.ap.*, left auricular appendage; *R.V.*, right ventricle; *R.A.*, right atrium; *L.V.*, left ventricle.

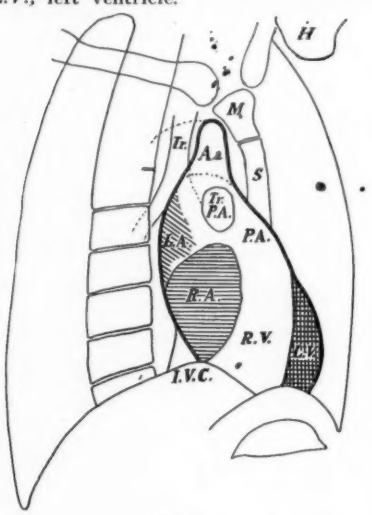

Fig. 2.

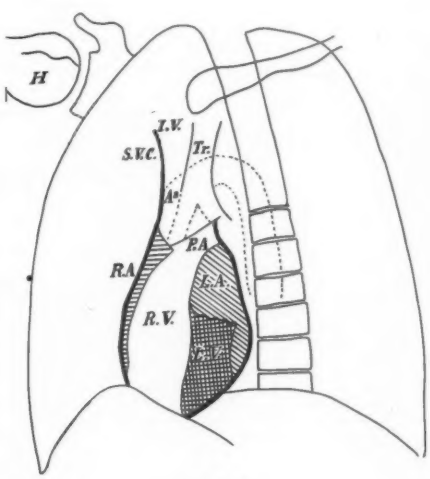

Fig. 3.

Fig. 2.—Diagram of the normal heart in the first oblique position. *I.V.C.*, Inferior vena cava; *L.A.*, left atrium; *Tr.*, trachea; *A.a.*, ascending aorta; *Tr. P.A.*, cross-section of the pulmonary artery; *P.A.*, pulmonary artery; *R.V.*, right ventricle; *L.V.*, left ventricle; *M*, manubrium; *S*, sternum; *H*, head of humerus.

Fig. 3.—Diagram of the normal heart in an exaggerated second oblique position. *R.A.*, Right atrium; *S.V.C.*, superior veno cava; *I.V.*, innominate vein; *A.a.*, ascending aorta; *P.A.*, pulmonary artery; *L.V.*, left ventricle; *Tr.*, trachea; *H*, humerus; *R.V.*, right ventricle.

so does ability to judge aortic width fluoroscopically increase after many examinations in the normal and pathological. For this reason it seems logical to depend upon experience and general impression

after fluoroscopy rather than on a number of figures subject to many unknown factors.

The differential diagnosis of the pathological aorta is one of the important problems awaiting a possible roentgenological solution. We have to differentiate, therefore, between the dilatation of atherosclerosis, advancing age, hypertension, aortic insufficiency and stenosis of the isthmus. I have had no experience with isthmus stenosis. A review of these syphilitic cases gives the definite impression that these lesions cannot always be safely differentiated roentgenologically. Yet a diagnosis can be safely made when the lesion is well marked, and this margin of safety increases notably when the clinical facts are used. Therefore, the roentgen diagnosis should always be accepted by the clinician with this condition—"provided the history and physical findings agree or at least do not oppose."

Of the forty cases there are three considered as early. These will be discussed as a separate group. The remaining cases showed changes which we all associate with a pathological aorta, namely:

1. A dense shadow often with hazy borders.
2. A high, dense and prominent aortic knob.
3. Irregular and also general dilatation.
4. Increased pulsation.
5. Association with aortic insufficiency.

In many of the cases the shadow was unusually dense, supporting previous reports that the luetic aorta produces a denser shadow than other lesions. This density is due for the most part to the increased diameter of the blood column incident to dilatation, and probably also in part to the changes in the wall. The changes in the height of the knob are most likely secondary to the changed spacial relations due to aortic elongation and dilatation. The most important sign is irregular dilatation. This presents itself as one or more localized spindle-shaped areas, not aneurysmal in dimension and involving most commonly the root. In the postero-anterior view, such a change appears as a dense shadow of the upper right cardiac arch (Fig. 4). Its border if extended would not conform to remaining portions of the silhouette. In the first oblique the anterior and posterior borders of the ascending aorta do not run parallel as normally, but, because of the greater dilatation of the root, they converge toward the aortic knob. Hence the silhouette is triangular with the base down. If the localized dilatation is near the knob, then the walls converge toward the heart and the silhouette becomes club-shaped. In the second oblique view, because the course of the aorta is now at right angles to the path of the rays, making the entire silhouette visible especially in the pathological case, local dilatations can easily be made out (Fig. 5). These local dilatations are to be expected, and they are easily explained by the disruption of the elastic fibers so common in syphilitic

aortitis. With the dilatation there is a localized increase in pulsation which should always be looked for and used as an index to dilatation.

In the later stages dilatation may become diffuse (Fig. 6). This can become extreme, and since marked dilatation is seldom seen in

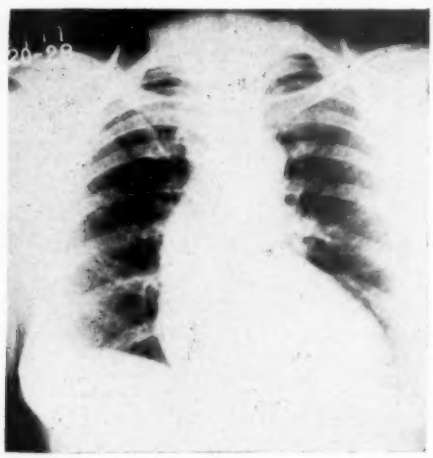

Fig. 4.—Localized dilatation of the ascending aorta as seen in the postero-anterior view.

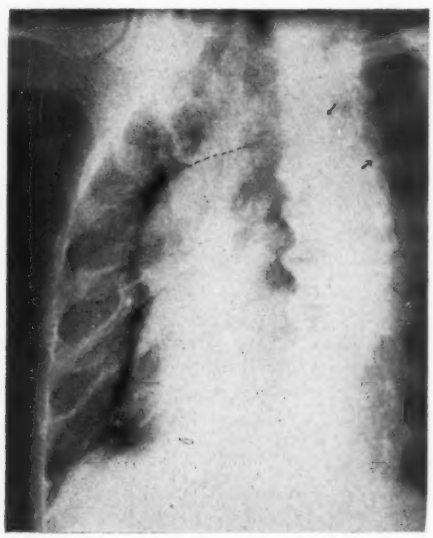

Fig. 5.—Localized dilatation of the ascending portion. The arc of this portion when continued (----) does not conform to the remaining portions of the arch (arrows).

other lesions, it has considerable diagnostic importance. The pulsations are decreased in amplitude, probably due to cicatricial changes. Increasing dilatation on repeated observation tends to rule out atherosclerosis in favor of syphilitic aortitis.

To summarize the well-marked cases of syphilitic aortitis, it can be said that the findings of a high, dense and prominent knob, a slight haziness in outline, a cardiac silhouette consistent with aortic insuffi-

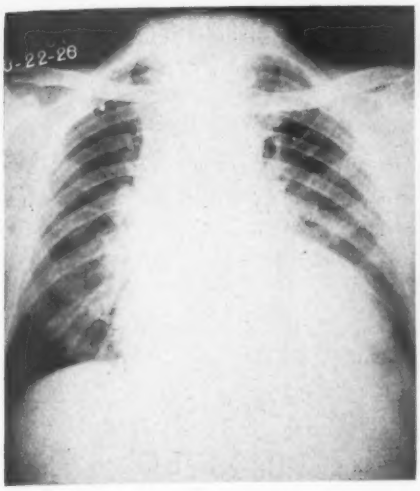

Fig. 6.

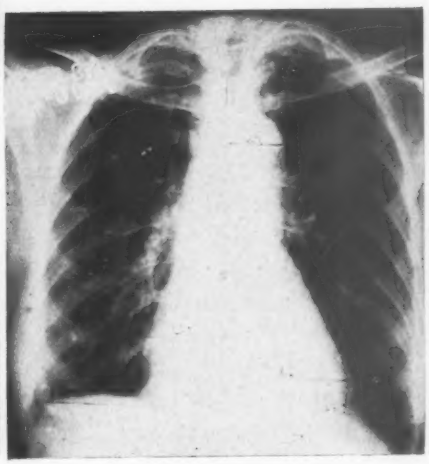

Fig. 7.

Fig. 6.—Diffuse dilatation of the aorta with aortic insufficiency.

Fig. 7.—Early case. Aortic insufficiency. Autopsy seven days after this examination.

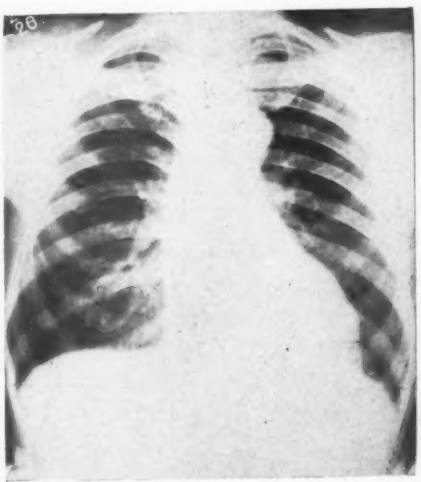

Fig. 8.

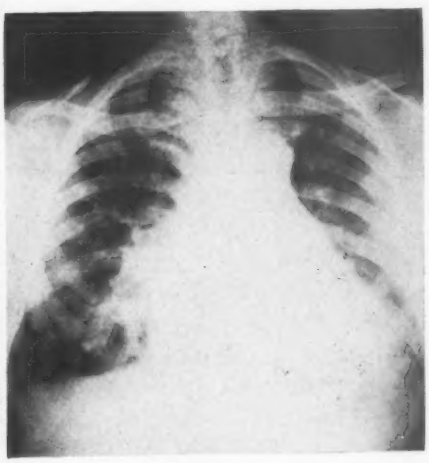

Fig. 9.

Fig. 8.—Early case. Fluoroscopically the ascending portion of the aorta was locally dilated and showed increased pulsations. See next figure for follow-up examination.

Fig. 9.—The same case showing diffuse dilatation of the aorta and cardiac decompensation.

ciency, generalized dilatation, unless excessive, and increase in amplitude of pulsation are not in themselves pathognomonic signs for the

roentgenological diagnosis of syphilis. A marked degree of generalized dilatation is more common in syphilis and can be taken as presumptive evidence, especially if the heart shadow is small or if it occurs in a person under forty. When the various segments are variably dilated the diagnosis is almost certain. I say "almost" because Vaguez and Bordet report local dilatation of the aortic root in Hodgkin's disease. Rheumatic dilatation has been reported also. The roentgen findings should always be correlated with the clinical and laboratory findings. However, too great reliance must not be placed on the Wassermann test, because in this series of thirty-six cases so examined, fourteen, or about 39 per cent, were negative and four, or 11 per cent, were reported as anticomplementary.

The three cases referred to above represent the earliest lesions of the series and are characterized by minimal or questionable roentgenological changes in spite of the fact that at autopsy the lesion was well marked. Each case shows an increase in the height of the knob and an increased density, changes which *per se* are found in the other common lesions. When these are present alone, which is true of two of these three, the diagnosis of syphilis is not possible. However, in each case, the right upper cardiac arch has a hazy outline and shows an indefinite or questionable bulge to the right. In one case there was present in the second oblique position a slight localized dilatation with increased pulsation in the ascending aorta (Fig. 7). The significance of the hazy outline and the very questionable bulging of the right upper arch in the postero-anterior view is questionable, but seeing such a change should call for very careful fluoroscopic observation in the second oblique view for localized dilatation and pulsation. When these findings are demonstrable, the diagnosis rests upon a firm foundation. Fig. 4 represents a well-marked localized dilatation of the ascending aorta in the postero-anterior view, and Fig. 5 represents similar changes in the second oblique position. If the arc of the dilated portion is schematically continued, it will be noticed that it does not conform to the remaining outline of the arch. We must conclude, therefore, that early syphilitic aortitis is not always demonstrable roentgenologically and that its earliest sign is localized dilatation associated with a localized increase in the amplitude of the pulsations (Figs. 8 and 9).

SUMMARY

There are cases of syphilitic aortitis which present definite roentgenological changes and which are indistinguishable from the other common lesions of the aorta. The lesions can be suspected when (1) a diffuse dilatation is present and is associated with a normal sized heart silhouette, (2) a dense, high aorta is present in a young individual without a previous hypertension. It can be safely diagnosed when

localized dilatation associated with localized increased pulsation is demonstrable.

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DISCUSSION

Dr. Lee, Washington, D. C.—Dr. Steel referred to the size of the heart. Does he use the measurements of Bordet and Vaquez, and in what phase of respiration does he take the pictures?

Dr. Lewis A. Conner, New York, N. Y.—I do not feel that I can let this opportunity pass without adding a warning concerning the roentgenological diagnosis of syphilitic aortic disease. I think Dr. Steel has been very conservative in his statements. It seems to me, however, that it would be a pity for us to go away with the idea that this is a safe method of establishing a diagnosis. I have frequently seen the grossest sort of mistakes made because of too great reliance upon the roentgenographic and fluoroscopic appearances of the aorta. I do not think one is often justified in making that diagnosis on the basis of the roentgenological findings alone, and I am sure Dr. Steel does not think so. This is no criticism of his statements. Elongation of the aorta begins very early and is very frequent in the early fifties even without any outstanding hypertension, and doubtless there are also variations in the curves of the right and left side of the heart, but most of us are not skilled enough to use these slight signs as important factors in the diagnosis. I still believe, as I have for many years, that clinical diagnosis of syphilitic aortitis, in the absence of aneurysm and other gross deformities of the aorta, cannot safely be established before the advent of aortic insufficiency.

Dr. W. S. Thayer, Baltimore, Md.—One word in connection with Dr. Conner's remarks. The only way we can establish a diagnosis is by finding out all that we can from every source, and then by putting our heads together. The man who is attempting to make a definite diagnosis on the basis of one single method of examination, is doing a very rash thing. I think this method is an admirable one, but I would like to say more than Dr. Conner, and that is that we clinicians should

consult with our consultants, whether laboratory men or roentgenologists, and get information from every source. We cannot make a diagnosis on only one finding.

Dr. W. W. Hamburger, Chicago, Ill.—Does filling the esophagus with a heavy barium mixture add materially to the x-ray diagnosis of syphilitic aortitis?

Dr. Steel (closing).—I think the essence of the paper has been well understood. Conservatism is the keynote and hence the diagnosis of syphilitic aortitis by the roentgenologist alone should always be accepted by the clinician with the proviso "provided the history and clinical findings agree or at least do not oppose." Plates are taken in mid-inspiration.

FLUOROSCOPIC STUDIES OF THE HEART AND AORTA IN ACQUIRED AND CONGENITAL SYPHILIS

CHESTER M. KURTZ, M.D., AND J. A. E. EYSTER, M.D.
MADISON, WIS.

THE present study was undertaken for the purpose of determining, by means of physical and fluoroscopic examination, the presence and degree of cardiovascular involvement in the various types and stages of syphilitic disease. It is rather generally believed and taught that there are several strains of spirochetes each one of which is more or less selective, and that the system attacked, whether it be cardiovascular, central nervous or skeletal, depends upon the type of invading organism. With this in mind, special attention was given to a group of patients suffering primarily from syphilis of the central nervous system, and the cardiovascular findings of this group will be treated separately.

FLUOROSCOPIC APPEARANCE OF THE AORTA

In the normal individual below the age of fifty years, the ascending aorta can be visualized in all views and, in the frontal plane, can be seen lying directly behind and projecting somewhat to the left of the sternum, extending from the level of the first rib to about the third rib. The right border of the shadow cast by the great vessels is ordinarily composed of the venae cavae and shows no definite pulsation. The descending aorta normally cannot be visualized. As the age of fifty years is approached, however, certain changes begin to take place. The aorta loses some of its elasticity, becomes slightly elongated, and increases in density. As a result, the fluoroscope reveals some sagging of the ascending aorta to the right with pulsation visible to the right of the sternum, and there is a sufficient increase in density to enable the observer to visualize the descending aorta in the lateral and oblique views, and in many cases in the frontal view as well. Above the age of fifty years these changes increase progressively, and the degree of tortuosity and density depends upon the extent of the degenerative changes which are taking place.

If these changes can be demonstrated in a person below the age of fifty years, say in the thirties or early forties, it can be assumed in the great majority of cases, at least, that an infectious process of some kind has attacked the aorta producing a certain degree of aortitis. In patients more than fifty years old, one has to use a certain amount of judgment in deciding whether the changes are in excess of what might be expected at that age.

In cases where the aortitis has progressed to such an extent that aneurysm formation has occurred, a localized area of sacculation can be visualized under the fluoroscope and the diagnosis definitely confirmed.

In the present study the diagnosis of the presence of aortitis, and the degree (slight, moderate, or marked) were based upon the points above mentioned: the shape of the ascending aorta, the presence of pulsation to the right of the sternum, and the density of the descending aorta. A diagnosis of aneurysm was made whenever a localized area of sacculation could be visualized in any portion of the aorta.

CASES STUDIED IN THE PRESENT SERIES

The series is composed of 54 cases of acquired syphilis and 12 cases of congenital syphilis seen at the Wisconsin General Hospital, including both ward patients and outpatients. Of the 54 cases of acquired syphilis, 40 were males and 14 females. The ages ranged from eighteen to seventy-four years with an average of forty-seven years. Four of the females and 11 of the males denied all knowledge of any syphilitic infection, making it impossible to determine the duration of the disease in 27.8 per cent of the cases. In the remaining cases, the duration of the infection ranged from four months to forty-nine years, with an average of twenty years. The large majority were charity patients who came chiefly from the lower strata of society. In only 2 of the whole group could the previous antiluetic therapy have been considered as adequate, and in the remaining 52 cases treatment had been decidedly inadequate or lacking altogether.

The congenital group consisted of 4 males and 8 females, ranging from nine to thirty-three years of age, with an average age of nineteen years. Seven of these cases had received no antiluetic therapy whatever at the time of admission to the hospital, and the other five had been adequately treated only for the past three or four years.

All the cases included in this series were known to have syphilis, either from history, finding of definite syphilitic lesions, a positive Wassermann reaction or some combination of these. Any doubtful cases, or cases complicated by rheumatic heart disease, were excluded.

A complete study was made of each patient, including history, physical examination, orthodiagram, and electrocardiogram. The blood Wassermann reaction was determined in every case, and the spinal fluid was examined in about two-thirds of the cases. The heart size was determined by the orthodiascopic method, the frontal area and transverse diameter being measured and compared with the predicted normal as calculated on the basis of the age, height and weight of the individual. The deviation from the predicted normal was expressed in percentage, and the normal range was considered to lie within the limits of plus and minus 10 per cent.

RESULTS

Table I gives a summary of the findings in the group with acquired syphilis.

Incidence of Aortitis.—Of the 40 males in the acquired syphilitic group, only 2 showed no evidence of aortitis. One of these had been infected two years and the other fifteen years previously. Neither had received adequate treatment. An aortitis of slight degree was found in 11 (27.4 per cent), moderate in 13 (32.5 per cent), and marked in 14 (35.1 per cent). Of the 14 females, 3 showed no evidence of aortitis. Two of these were still in the secondary stage having been infected less than three months, and the third gave no history of a primary lesion, thus rendering it impossible to determine the duration. Of the remaining 11, an aortitis of slight degree was found in 2, moderate in 7, and marked in 2. Aortitis of some degree was found in 95 per cent of the males, 78.6 per cent of the females, or 90.7 per cent of the total. Nineteen of the males were fifty years old or over, and of these the aortitis was considered to be consistent with the age of the patient in 6 cases, and more marked than would be expected in 13. Five of the females were fifty years old or over, and of these 2 showed an aortitis consistent with the age, while 3 showed a more marked process.

The period required for the development of a demonstrable degree of aortitis appears to be very variable. In one man of twenty-one years, who had received his initial lesion two years previously and who had been treated over a period of nine months, no aortitis was found. Another man, twenty-six years of age, who had been infected two and one-half years before and who had received treatment for eighteen months following the primary lesion, showed evidence of an early aortitis. A third man, fifty-one years old, who had contracted the disease fifteen years before, and who had received very inadequate treatment had no signs of aortitis.

Of the four males in the congenital group (Table II), only one showed no evidence of aortitis, while the other 3 exhibited early signs and were classified as slight. Of the eight females with congenital syphilis, 6 had no signs of aortitis, while the remaining two were classified as having a moderate degree. These two were aged twenty-two and thirty-three years respectively, and with one exception were the oldest of the group. The oldest of those not showing signs of aortitis was twenty-four. Fifty-eight and four-tenths per cent of all the congenital cases showed no signs of aortitis, leaving 41.6 per cent with evidence of a slight or moderate degree. A marked degree of aortitis was not found in any of this group.

Incidence of Aneurysm.—A diagnosis of aortic aneurysm was made in 7 of the males with acquired syphilis, and in 3 of the females, making a total of 10, or 18.5 per cent. The earliest period at which an

TABLE I

FLUOROSCOPIC FINDINGS IN FIFTY-FOUR CASES OF ACQUIRED SYPHILIS

NO. OF CASES	AGE YEARS		DURATION OF INFECTION		FLUOROSCOPIC EVIDENCE OF AORTITIS								ANEURYSM		HEART SIZE					
	LIMITS	AVE.	LIMITS	AVE.	NONE		SLIGHT		MODERATE		MARKED				SMALL		NORMAL		ENLARGED	
					NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males																				
40	21-74	49	2-49	22.4	2	5.0	11	27.4	13	32.5	14	35.1	7	17.5	5	12.5	18	45.0	17	42.5
Females																				
14	18-60	40	⅓-22	12.0	3	21.4	2	14.3	7	50.0	2	14.3	3	21.4	5	35.7	5	35.7	4	28.6
Total																				
54	18-74	47	⅓-49	20.0	5	9.3	13	24.1	20	37.0	16	29.6	10	18.5	10	18.5	23	42.6	21	38.9

TABLE II

FLUOROSCOPIC FINDINGS IN TWELVE CASES OF CONGENITAL SYPHILIS

NO. OF CASES	AGE YEARS		FLUOROSCOPIC EVIDENCE OF AORTITIS								ANEURYSM		HEART SIZE					
	LIMITS	AVE.	NONE		SLIGHT		MODERATE		MARKED				SMALL		NORMAL		ENLARGED	
			NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males																		
4	9-30	18	1	25.0	3	75.0	0	0	0	0	0	0	2	50.0	2	50.0	0	0
Females																		
8	12-33	20	6	75.0	0	0	2	25.0	0	0	0	0	2	25.0	6	75.0	0	0
Total																		
12	9-33	19	7	58.4	3	25.0	2	16.6	0	0	0	0	4	33.3	8	66.7	0	0

aneurysm was found was twelve years after the onset of the disease. One woman of thirty years who had been infected twelve years previously and had received almost no treatment, had a small aneurysm of the ascending aorta. A man of fifty-two years who gave a history of an initial lesion twelve years before, had a large aneurysmal sac of the ascending aorta. In the other cases in which aneurysm was found, the duration of the infection ranged from twenty-two to thirty-two years. None of the congenital cases showed any signs of sacculation.

Heart Size.—As previously explained, the frontal area and the transverse diameter of the heart were orthodiagraphically measured in each case and compared with the predicted normal. Table I shows the variation in the heart size in the various groups. Cardiac enlargement (area above +10 per cent) was present in 17 (42.5 per cent) of the males, and in 4 (28.5 per cent) of the females, making a total of 21, or 38.9 per cent, of the entire group. Five of the males and an equal number of the females had hearts below −10 per cent in area, making a total of 10, or 18.5 per cent. The heart size lay within the normal range (−10 to +10) in 18 of the males and 5 of the females making a total of 23, or 42.6 per cent. In the congenital group, none of the hearts were found to be enlarged. Seven (63.6 per cent) were in the normal range while 4 (36.4 per cent) were below normal size.

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

Of special interest was a group of 23 patients, 19 males and 4 females, who were suffering primarily from syphilis of the central nervous system, and who were on the neurological service with diagnoses of general paresis, tabes dorsalis, taboparesis and meningovascular syphilis. The findings for this group are summarized in Table III. These patients ranged from thirty to sixty-two years of age, with an average of forty-five years. The average duration of the infection was twenty years, the limits being ten and twenty-six years. None of these had been adequately treated previously. Aortitis could be demonstrated in all of the males and in 3 of the 4 females, making a total of 22, or 95.7 per cent. Four males and 1 female showed a definite aneurysm of the aorta, making a total of 5, or 21.8 per cent. It is unsafe to draw conclusions from such a small number, but it is interesting to note that in this particular series the group classed as syphilis primarily of the central nervous system showed a higher incidence of aortitis and aneurysm than did the entire group composed of patients with acquired syphilis of all types. Only 7 (30.2 per cent) showed cardiac enlargement. In 13 (56.7 per cent) the heart size was within the normal range, and 3 (13.1 per cent) had hearts below normal size. Sixteen (69.7 per cent) showed definite cardiac involvement clinically, and aortic regurgitation was present in 3 (13.1 per cent) of this group.

TABLE III

FLUOROSCOPIC FINDINGS IN TWENTY-FOUR PATIENTS WITH SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

NO. OF CASES	AGE YEARS		DURATION OF INFECTION		FLUOROSCOPIC EVIDENCE OF AORTITIS								ANEURYSM		HEART SIZE					
	LIMITS	AVE.	LIMITS	AVE.	NONE		SLIGHT		MODERATE		MARKED				SMALL		NORMAL		ENLARGED	
					NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males																				
19	36-62	47	10-26	21	0	0	7	36.8	6	31.6	6	31.6	4	21.0	1	5.2	12	63.2	6	31.6
Females																				
4	30-54	45	12-20	16	1	25.0	1	25.0	2	50.0	0	0	1	25.0	2	50.0	1	25.0	1	25.0
Total																				
23	30-62	46	10-26	20	1	4.3	8	34.8	8	34.8	6	26.1	5	21.8	3	13.1	13	56.7	7	30.2

TABLE IV

CLINICAL FINDINGS IN FIFTY-FOUR CASES OF ACQUIRED SYPHILIS

NO. OF CASES	AGE YEARS		DURATION OF INFECTION		ANTILUETIC TREATMENT		AORTIC REGURG.		CARDIAC INVOLVEMENT		BLOOD PRESSURE				POSITIVE WASSERMANN				CNS LUES	
	LIMITS	AVE.	LIMITS	AVE.	ADEQUATE	INADEQUATE					NORMAL		ELEVATED		BLOOD		SP. FLUID			
							NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%*	NO.	%
Males																				
40	21-74	49	2-49	22.4	1	39	7	17.5	29	72.5	31	79.5	8	20.5	23	59.0	14	46.7	20	50.0
Females																				
14	18-60	40	1/3-22	12.0	1	13	2	14.3	10	71.5	9	75.0	3	25.0	11	78.6	4	57.2	5	35.7
Total																				
54	18-74	47	1/3-49	20.0	2	52	9	16.6	39	72.3	40	78.5	11	21.5	34	63.0	18	48.7	25	44.5

*Per cent of cases in which spinal puncture was done.

TABLE V

CLINICAL FINDINGS IN TWENTY-THREE CASES OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM

NO. OF CASES	AGE YEARS		DURATION OF INFECTION		ANTILUETIC TREATMENT		AORTIC REGURG.		CARDIAC INVOLVEMENT		BLOOD PRESSURE				POSITIVE WASSERMANN			
	LIMITS	AVE.	LIMITS	AVE.	ADEQUATE	INADEQUATE					NORMAL		ELEVATED		BLOOD		SP. FLUID	
							NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males																		
19	36-62	47	10-26	21	0	19	2	10.5	13	68.5	17	94.7	1	5.3	11	58.0	13	68.5
Females																		
4	30-54	45	12-20	16	0	4	1	25.0	3	75.0	4	100.0	0	0	1	25.0	4	100.0
Total																		
23	30-62	46	10-26	20	0	23	3	13.1	16	69.7	21	95.5	1	4.5	12	52.2	17	74.0

TABLE VI

CLINICAL FINDINGS IN TWELVE CASES OF CONGENITAL SYPHILIS

NO. OF CASES	AGE YEARS		ANTILUETIC TREATMENT		AORTIC REGURG.		CARDIAC INVOLVEMENT		BLOOD PRESSURE				POSITIVE WASSERMANN				CNS LUES	
	LIMITS	AVE.	ADEQUATE	INADEQUATE					NORMAL		ELEVATED		BLOOD		SP. FLUID			
					NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Males																		
4	9-30	18	0	4	0	0	0	0	4	100.0	0	0	4	100	2	50.0	3	66.7
Females																		
8	12-33	20	0	8	0	0	3	37.5	7	87.5	1	12.5	8	100	2	25.0	4	50.0
Total																		
12	9-33	19	0	12	0	0	3	25.0	11	91.7	1	8.3	12	100	4	33.3	7	58.4

MISCELLANEOUS

A number of items of interest, such as the incidence of cardiac involvement, aortic regurgitation, hypertension, and positive Wassermann reactions for the entire group, which lie outside the scope of this paper, will be found recorded in Tables IV, V and VI, and may be of some value to those working on other phases of this subject. The heart was considered to be involved whenever there was cardiac enlargement, physical signs of heart disease, or definite electrocardiographic changes. A diagnosis of hypertension was made whenever the systolic pressure was over 150 or the diastolic over 100 mm. of mercury.

GROUP OF QUESTIONABLE ETIOLOGY

During the course of this study seven cases came under observation, in which there was a demonstrable degree of aortitis but no history or clinical evidence of either syphilitic or rheumatic infection. There were 4 males and 3 females, the ages ranging from eighteen to fifty years, with an average of thirty-five years. The degree of involvement was slight in 2, moderate in 4 and marked in 1. All but one had cardiac symptoms. Aortic regurgitation was present in 2, and the heart showed slight involvement in one case, moderate involvement in 3, marked involvement in 1, and appeared normal in 2. The patient who had no symptoms was a girl of eighteen years, with aortic regurgitation, a moderate degree of aortitis, fairly marked cardiac enlargement and a definitely pathological electrocardiogram. One woman of fifty years, with negative past history, had an aortitis definitely more marked than would be expected at that age, and the electrocardiogram showed a bundle-branch block. The blood Wassermann was repeatedly negative, and there was no other evidence of a syphilitic infection. Another case, a man of fifty years, with aortic regurgitation, had a small aneurysm of the ascending aorta, and the electrocardiogram showed complete heart-block. As in the rest of this group, the Wassermann reaction was negative, and no other evidence of syphilis could be found. No explanation for these cases is offered, but the question is brought up as to whether there may not be some other etiological factor in the production of changes in the aorta in addition to those with which we are familiar at the present time.

NECROPSIES

Three of the patients in the acquired syphilitic group died in the hospital and came to autopsy. The first case, a man of fifty years who gave a history of an initial lesion twenty-five years before, was on the neurological service with a diagnosis of tabes dorsalis. Cardiac symptoms were marked. On fluoroscopic examination the aorta was found

to be greatly dilated and a large aneurysm of the transverse arch could be visualized. The patient later died of heart failure and at post-mortem examination two aneurysms were found, one of the transverse arch and a very large one in the descending aorta situated directly behind the heart in such a manner that on fluoroscopic examination the shadow of the aneurysm had fused with that of the heart to such an extent that it was impossible to distinguish them.

The second case was that of a man of fifty-three years who gave no history of a syphilitic infection and had never known he had the disease. The blood Wassermann was positive, and on fluoroscopic examination a marked degree of aortitis was noted, as well as a large aneurysm of the transverse arch. This patient later died of congestive failure, and post-mortem examination revealed a marked syphilitic aortitis with a large aneurysm involving the transverse arch and the first portion of the descending aorta.

The third case was that of a man of seventy-four years who gave a definite history of syphilitic infection forty-nine years before. He had received very little antiluetic therapy. He complained chiefly of dyspnea and a chronic cough. The blood Wassermann was positive. On fluoroscopic examination a marked degree of aortitis was found, but no aneurysm formation. A diagnosis of syphilitic aortitis was made. The patient later died, and at necropsy the aorta showed no evidence of a syphilitic process but a moderate degree of arteriosclerotic change. The cause of death was found to be primary carcinoma of the lung. This case was instructive in that it demonstrated the possibility of the aorta escaping involvement in the presence of a syphilitic infection with positive Wassermann over a period of nearly fifty years.

SUMMARY AND CONCLUSIONS

1. A series of 54 cases of acquired and 12 cases of congenital syphilis are presented with special reference to the fluoroscopic findings in the heart and aorta.

2. Fluoroscopic evidence of aortitis was found in 90.7 per cent of the cases of acquired syphilis and in 36.4 per cent of the cases of congenital syphilis.

3. Aneurysm of the aorta was found in 18.5 per cent of the cases of acquired syphilis and was absent in all of the congenital cases.

4. Cardiac enlargement was present in 38.9 per cent of the cases of acquired syphilis.

5. In a group of 23 cases of acquired syphilis, exhibiting primarily central nervous system disease, 95.7 per cent showed evidence of aortic involvement, and aneurysm could be demonstrated in 21.8 per cent.

DISCUSSION

Dr. L. A. Conner, New York, N. Y.—As I understand this, it was purely a fluoroscopic study. When therefore Doctor Kurtz says that a certain large percentage of the patients showed signs of syphilitic aortitis it seems to me he must mean that they showed changes from his conception of the normal fluoroscopic picture, which he interpreted as being evidences of aortitis. If that is the case I submit that the two things are not necessarily synonymous.

Dr. H. E. B. Pardee, New York, N. Y.—I would like to hear in more detail what were the criteria used for the diagnosis of aortitis in this report.

Dr. Kurtz (closing).—I used the term aortitis in a broad sense to denote any demonstrable changes in the aorta, the criteria for such a diagnosis being: (1) elongation or tortuosity, (2) widening of any portion, (3) pulsation to the right of the sternum, and (4) increased density permitting visualization of the descending aorta, especially in patients under the age of fifty years. It is ordinarily not possible to distinguish between the syphilitic and arteriosclerotic types of aortitis on fluoroscopic examination. This was well illustrated in the case mentioned at the close of the paper. The patient was a man of seventy-two years who gave a definite history of syphilitic infection about fifty years previously. The blood Wassermann was positive, and on fluoroscopic examination the aorta showed very definitely the changes which are ordinarily associated with an aortitis. I boldly made a diagnosis of syphilitic aortitis, but when the patient died and came to autopsy, the process was purely arteriosclerotic in type, and no syphilitic changes were found. Since then I have been careful not to make an etiological diagnosis on the basis of fluoroscopic appearance. The only difference in the appearance of the aorta with aneurysm is a localized sacculation in addition to the other criteria mentioned above.

FURTHER STUDIES OF THE AORTA WITH SPECIAL REFERENCE TO LUETIC AORTITIS

A. O. Hampton, M.D., E. F. Bland, M.D., and
Howard B. Sprague, M.D.
Boston, Mass.

A METHOD for determining the presence or absence of abnormal dilatation of the aorta has been a subject of considerable interest for both clinical and roentgenological investigators. Repeated attempts have been made at the Massachusetts General Hospital by various workers to standardize some practical method of determining the size of the ascending and transverse portion of the thoracic aorta.

In this paper we are continuing the study recently reported by Hampton and Jones[1] in which a method was presented for the determination of aortic dilatation. In the earlier paper the left anterior oblique view of the aorta taken at seven feet tube-screen distance, with the aid of fluoroscopy at the same distance, was reviewed in a selected group of 120 cases. In this group, 84 patients were suspected clinically of having luetic aortitis. Seventeen other cases were selected because the aorta appeared to be visible in the left anterior oblique teleroentgenogram. None of these latter cases was considered clinically abnormal except for the presence of arteriosclerosis. The age group of the 17 cases ranged from forty to sixty years, being well within the usual luetic aortitis age limit. In the remaining 19 cases of the group of 120, hypertension was considered to be the cause of aortic dilatation, although 4 had positive Wassermann reactions and 7 had aortic regurgitation. The result of the above investigation seemed to justify the deduction of a normal and abnormal average measurement of the aortic root shadow and aortic arch. The arteriosclerotic aortic root shadow was found to be no more than 6 cm. in diameter and in the dilated aorta group was invariably over 6 cm. in diameter. A clinical and roentgenological agreement of 79.8 per cent of the cases was established.

The method employed in the present study is the same as the one previously described by Hampton and Jones.[1]

Standard teleroentgenograms are taken of each case studied with the patient in three positions: antero-posterior, right anterior oblique and left anterior oblique, of which the latter has been found to be the most valuable.

For the left anterior oblique view, the patient is placed at an angle of from forty to fifty degrees with the central beam of the x-ray. This position is best obtained by direct observation with seven foot fluoroscopy. Under direct roentgenoscopic observation, the patient is rotated to the right with the left nipple and left shoulder in approximation with the fluorescent screen until the bright space behind the ascending aorta and below the aortic arch is most clearly seen. The right arm is then brought forward over the top of the screen, the right wrist of the

patient is grasped by the examiner and rotated medially as it is pulled upward and forward. Care must be taken to maintain the semilateral position. This maneuver results in drawing the right scapula forward and upward and causes the right intercostal spaces to widen, thus giving the maximum clearness of the aorta in so far as it is visible. The fluoroscopic screen is then replaced by the radiographic cassette. The tube is centered at the fourth dorsal vertebra. The patient is instructed to take and hold a deep breath. The exposure time should be as short as possible, preferably 1/10th to 1/20th of a second. The fluoroscopic observation of the pulsation and relative size of the aorta together with the impression obtained during the course of the examination is very important. A seven foot fluoroscope is not necessary for proper posing of the patient. Many satisfactory examinations have been made without its use. The right oblique view of the aorta is obtained in much the same manner except that an effort is made to superimpose the ascending and descending aorta by rotating the patient in the opposite direction, the proper angle between the line of the shoulders and the central beam being approximately thirty degrees.

Measurements of the supracardiac shadow obtained from the teleroentgenogram are made in the anteroposterior and left anterior oblique views. The anteroposterior projection is measured by a transverse line across the widest point of the supracardiac silhouette above the region of the pulmonary artery. The aorta is considered to be abnormal if this transverse measurement exceeds 6 cm. and is not explained by tortuosity of the aorta, obesity, high diaphragm, or mediastinal mass.

The radiograph obtained with the patient in the left anterior oblique position must be carefully studied. It is necessary to identify the arch of the aorta, the trachea, and the posterior border of the heart. The arch is best seen where it is crossed by the trachea and left main bronchus. The posterior border of the heart can usually be traced upward from the apex to the region of the pulmonary artery. The inferior margin of the arch of the aorta is then followed anteriorly and downward to the region of the pulmonary artery where it intersects the posterior border of the heart. This is often difficult unless the radiograph is of excellent quality and the examiner has had considerable experience. The pulmonary artery should be identified if possible, and when there is no doubt of its identity, the method of measurement suggested by O'Kane, Andrew, and Warren[2] has been found to be valuable. When the pulmonary artery is not visualized, as is often the case, the visible portions of the posterior border of the ascending aorta must be projected downward to meet the line of the posterior border of the heart. This intersection is in the anatomical location of the pulmonary artery and is taken as the posterior point of a transverse line to be drawn from the junction of the ascending aorta with the anterior border of the heart. The shadow of the anterior margin of the ascending aorta and the curve of the silhouette of the anterior border of the heart are easily identified. The length of the transverse line drawn between the above points rarely exceeds 6 cm., unless the aorta is abnormally dilated. It must be borne in mind that this diameter is not the true diameter of the aorta as it is found at post-mortem examination. It is merely an arbitrary measurement of the aortic root shadow which we believe to vary directly as the diameter of the aorta. We do not know the absolute diameter of the aorta as it exists when the arterial blood pressure is maintained, since such a direct measurement has rarely if ever been made. The diameter of the normal aorta as measured at post-mortem examination is not usually over 3 cm. The arch of the aorta may be measured in most cases, and this diameter does not exceed 3.5 cm. unless the aorta is dilated.

Using the above method, we have studied for the present report an additional series of 89 cases referred for roentgenological examination of the heart and great vessels because cardiovascular disease was sus-

Fig. 1-*A*.

Fig. 1-*B*.

Fig. 1 *A* and *B*.—*A*, Antero-posterior teleroentgenogram of arteriosclerotic aorta showing tortuosity without dilatation. *B*, Oblique teleroentgenogram of arteriosclerotic aorta. The aorta is unusually well shown. The measurements are within normal limits. Note points of measurement of ascending and arch portions of the aorta.

Fig. 2-*A*.

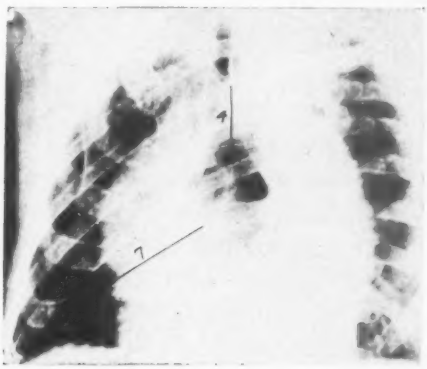

Fig. 2-*B*.

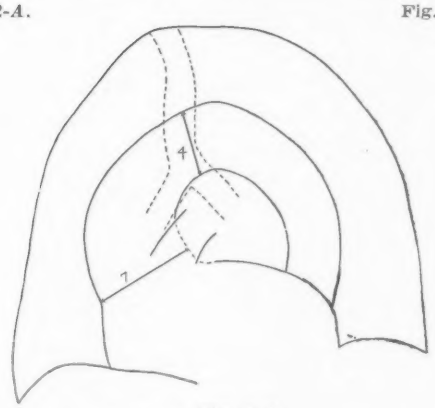

Fig. 2-*C*.

Fig. 2 *A*, *B* and *C*.—*A*, Antero-posterior teleroentgenogram of a dilated aorta. *B*, Left anterior oblique teleroentgenogram showing typical measurements of ascending and arch portions of the aorta. *C*, Tracing of *B*, showing typical measurements.

pected clinically. These examinations were done routinely in an effort to determine whether or not the measurement of the aortic root shadow in the left anterior oblique view is sufficiently reliable to be of practical value. The measurements were done before a correlation with clinical impressions had been made. This nonbiased attitude of the examiner was suggested as a contrast to that in the study of 120 cases previously reported in which a dilated aorta was anticipated in a relatively large percentage.

MEASUREMENT OF AORTIC ROOT SHADOW AND ARCH

Number of cases	89
Number of cases with abnormally dilated aorta by roentgen-ray examination	15
A. Clinically diagnosed luetic	11
B. Nonluetic	4

	AORTIC ROOT SHADOW ASCENDING AORTA	ARCH
Average transverse diameter of the 11 luetic aortas	7.0 cm.	4.6 cm.
Average transverse diameter of the 4 nonluetic dilated aortas	6.8 cm.	3.7 cm.
Average transverse diameter of nondilated aortas	5.3 cm.	3.3 cm.
Maximum normal transverse diameter	6.0 cm.	3.5 cm.

In the left anterior oblique view of the 89 cases, the transverse measurement of the aortic root shadow or ascending aorta exceeded the normal in 15, of which 11 were considered syphilitic, 2 had definite hypertension, 1 had marked arteriosclerosis, and 1 had arteriosclerosis and slight aortic regurgitation. Of the 11 cases with dilatation of the aorta by roentgenological examination, and in which lues was clinically considered the etiological factor, 6 had both a positive Hinton reaction of the blood serum and an aortic regurgitation. In 3 cases, the x-ray demonstration of a dilated aorta together with a positive Hinton reaction seemed sufficient evidence to warrant the clinical diagnosis of luetic aortitis in the absence of other possible etiological factors, such as hypertension or arteriosclerosis. In the remaining 2 patients, the presence of aortic regurgitation with a history of primary syphilitic infection even in the absence of a positive reaction of the blood serum was considered sufficient evidence for a diagnosis of luetic aortitis. The 4 remaining cases with the transverse measurement of the ascending aorta exceeding 6 cm., 2 had hypertensive heart disease, and 2 had arteriosclerotic heart disease clinically. It is of considerable interest that there were in this series 33 cases with definite hypertension but that only 2 showed evidence of aortic dilatation.

SUMMARY

The method of study of the aorta now in use at the Massachusetts General Hospital is presented. This method, we believe, is valuable in determining the presence or absence of aortic dilatation even in cases

where the clinical impression is not known to the roentgenologist. Roentgenoscopy at a seven foot tube-screen distance is considered a valuable aid to accurate positions for the teleroentgenogram. Teleroentgenography in the left anterior oblique position has been found to give valuable evidence of aortic dimensions. The points of measurement selected are described and are thought to be of practical application.

Measurements of the aorta in a series of routine radiographs compared with the clinical findings seem to justify the deduction of a normal and abnormal average. The normal and arteriosclerotic ascending aorta without dilatation was found to average 5.3 cm. The dilated ascending aorta invariably measures over 6 cm. in diameter when estimated by the method presented. The differential diagnosis in cases found by roentgen examination to have aortic dilatation depends upon clinical and other roentgen findings.

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THE ELECTROCARDIOGRAM AND TELEROENTGENOGRAM IN EARLY SYPHILIS*

RUTH INGRAHAM, M D., AND EDWIN P. MAYNARD, JR., M.D.
BROOKLYN, N. Y.

WHEN one studies the literature dealing with the heart and aorta in early syphilis, one finds great divergence of opinion as to the frequency with which clinical, electrocardiographic and x-ray evidence of involvement of these organs is to be found. The earlier writers in general seemed to find symptoms and signs of invasion of the heart and aorta in a much higher percentage of the early cases than do the more recent investigators. This is quite striking and suggests the thought that the change may be due, not only to better instruments of precision, but also to the use of more rigid criteria for the diagnosis of syphilis of the heart. For example, Grassman[1] in 1900 detected arrhythmia in 85 per cent, and murmurs in 40 per cent of 288 cases of secondary syphilis. Harlow Brooks[2] in 1921 found that out of 300 cases of syphilitic heart disease, 8 per cent showed cardiac involvement in the secondary stage. Howard[3] in 1924 stated that of fifty patients in the secondary stage, eight complained of palpitation, five of cardiac pain, and three of dyspnea; one had edema. In 1926 Wilson, Wile, Wishart and Herrmann[4] said that "a study of about sixty patients with primary and secondary lues has convinced us that reliable clinical or electrocardiographic evidence of involvement of the heart or aorta during this stage of the disease is decidedly rare." Turner and White[5] in 1927 made a very careful study of fifty cases of primary and secondary syphilis. They excluded from their series all cases of rheumatic heart disease, arteriosclerosis, hypertension, hyperthyroidism, or any other condition that might affect the heart, and limited their cases to patients under forty years of age. A complete study of these cases, including history, physical examination, electrocardiogram and x-ray examination showed no definite clinical evidence of disease of the heart or aorta. Finally, Arnett[6] in 1928 found that organic cardiovascular disease was not demonstrably present in any of the twenty-five secondary syphilis patients studied.

Thus, it is apparent that the clinical diagnosis of syphilitic involvement of the heart and aorta in early lues was made much more frequently by the pioneer workers in this field than it is today.

In 1927, at the suggestion of Dr. Alfred Cohn, a study of syphilis of the heart and aorta was begun in the adult Cardiac Clinic at the

*From the Departments of Medicine and Radiology, the Brooklyn Hospital, Brooklyn, N. Y.

Brooklyn Hospital. The plan of work is somewhat as follows: Every patient admitted to the Brooklyn Hospital venereal disease clinic in whom a positive diagnosis of syphilis has been made is referred to the cardiac clinic for complete survey, including history, physical examination, x-ray of heart and electrocardiogram. The examinations are made by two men trained in cardiology, and the patients are enrolled in the cardiac clinic. Reexaminations are made at varying intervals, depending upon the conditions found, but all patients are reexamined at least once a year. It is planned to keep up this work indefinitely in order to study the development and course of syphilis of the cardiovascular system. The present study of the electrocardiogram and x-ray findings in early syphilis is a part of the research program.

In order to make our findings significant it was decided to select our cases very carefully. We chose for early cases only those who had had syphilis for a year or less, and we excluded all patients in whom the date of the initial lesion was not known. Second, in order to exclude the changes due to age, we limited our series to patients under forty years. Third, to rule out hypertension, we included no case with a systolic blood pressure over 140 mm. Lastly, we excluded all patients who gave a history of any other disease that might affect the heart, including rheumatic fever, chorea and hyperthyroidism. As a result, our study, which began with fifty-five early cases, rapidly dwindled to a total of twenty-seven that fulfilled all the requirements.

Of these 27 cases, 19, or 70.4 per cent, gave electrocardiograms that fell within the limits of normal, 8, or 29.6 per cent, showed a left axis deviation, including one with premature ventricular beats as well. Compared with the findings in the series of cases of early syphilis studied by Turner and White,[5] the incidence of left axis deviation is much higher. They found only one instance in fifty cases, or 2 per cent. Cohn[7] in an investigation of the size of the heart in soldiers in 1920 found that of 208 normal soldiers six showed signs of left ventricular preponderance, an incidence of 2.8 per cent. Proger and Davis[8] have recently published a study of axis deviation in normal hearts and found that 33 per cent showed a left axis deviation, varying from slight to marked degree. Our figure of 29.6 per cent in young adults with early syphilis corresponds very closely with this. The one instance of premature ventricular beats cannot safely be attributed to the syphilis because of the many factors that may cause this irregularity in young people. Therefore, when one considers the frequency with which left axis deviation may be found in normal hearts, one must conclude that our findings of 29.6 per cent in young adults with early syphilis falls within the limits of normal. This brings us to the conclusion that in our study of the electrocardiogram

in twenty-seven cases of early syphilis, no significant deviations from the normal were found.

Now let us turn to the examination of these hearts by the teleroentgenogram. The films were taken in the antero-posterior position at a six-foot distance from the target. The shadow measured for the aorta was that shadow seen immediately to the right and to the left of the spine in the region of the aorta. In those films in which the shadow to the right formed a straight line rather than a convex curve, it is very likely that we were not measuring the aorta but the vena cava, and that the ascending aorta was not seen. In measuring the size of the heart itself, the total transverse diameter was used and compared with the total diameter of the chest. A total diameter of the heart, 50 per cent of the total diameter of the chest, was considered the upper limit of normal. However, in the actual consideration of enlargement, the conformation of the chest and the position of the diaphragm were taken into account.

A total of twenty-three cases was studied in this way. Of these, ten were normal throughout. In not any of them was there any very striking change in the aortic shadow, but in six, or 26 per cent, there seemed to be slight but definite enlargement, especially of the ascending aorta.

When we attempted to correlate the electrocardiographic findings with the x-ray, we found that of the six cases of left axis deviation in which films were made, three were normal and three showed slight but definite enlargement of the aorta. The three cases of enlargement of the aorta that remained gave normal electrocardiograms. Therefore, there was no close correlation between electrocardiographic and x-ray findings in our series.

From a study of the x-ray films in the twenty-three cases of early syphilis we cannot state that the slight changes found in the aorta in six were due to the syphilis. It may be that changes such as these would be found in a similar series of normal individuals.

One point further we wish to emphasize. As stated before, we limited our series very carefully to individuals who had no other condition but syphilis. As we threw out case after case, the interesting changes in the electrocardiogram and x-ray film began to disappear, until finally when our series was perfect our abnormal findings disappeared.

SUMMARY AND CONCLUSIONS

1. A series of twenty-seven cases of early syphilis was studied electrocardiographically. The tracings were found to fall within the limits of normal.

2. Twenty-three of these cases were studied by teleroentgenogram. Six of them showed slight widening of the aorta which was not beyond the limits of normal deviation.

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DISCUSSION

Dr. Herrmann, New Orleans, La.—I have had a case of pericarditis in a middle-aged patient with a severe roseolar rash of acute syphilis. The signs cleared up promptly under intensive arsphenamine therapy. I believe this was an acute syphilitic pericarditis and suggestive evidence that the pericardium may be involved in early syphilis. The Wassermann is still positive, but there are no evidences of cardiovascular syphilis. There were very slight changes in the T-wave of the electrocardiograms.

Dr. F. N. Wilson, Ann Arbor, Mich.—Some years ago Dr. Wile had several cases of primary and secondary lues in which he felt that involvement of the heart had occurred. He suggested that I examine a series of patients from his clinic from this standpoint. I examined approximately fifty patients with primary and secondary lues, when first seen, and again after the first course of arsphenamine. A physical examination was made, and an electrocardiogram was taken on each occasion. In not one of these patients did I find anything that led me to suspect that the heart was involved. Most of the patients were young and had no disease other than the infection for which they came to the clinic.

Dr. John Wyckoff, New York, N. Y.—I would like to ask about the P-R intervals and the QRS complex in this series.

Dr. Maynard (closing).—We studied the P-R interval, the QRS, the T-wave and the S-T interval in all our cases. There were no changes from the normal. I am interested in Dr. Wilson's series. We have not made a clinical study of our cases of early syphilis. We have not seen pericarditis as mentioned by Dr. Herrmann.

SYMPTOMS AND CLINICAL COURSE OF SYPHILITIC AORTIC INSUFFICIENCY*

R. W. Scott, M.D.
Cleveland, Ohio

THIS paper deals with the clinical observations on 107 autopsied cases of syphilitic aortic insufficiency seen on the wards of the Cleveland City Hospital during the past ten years. During this time a particular effort was made to correlate the clinical aspects of this disease with the post-mortem findings, in the belief that such a combined clinical and pathological study which brought the pathologist to the wards as well as the clinician to the laboratory, afforded the best method of attacking some of the problems associated with latent syphilis as a cause of heart disease.

Before considering the following observations, I think it important to mention that they were made on a group of patients in the charity wards of a municipal hospital. For the most part the patients were from the working class and more than 50 per cent were negroes. Many patients had advanced heart failure when first seen.

Sex.—There were 92 males and 15 females, a proportion of approximately six to one.

Age.—The youngest patient was twenty-three years old; the oldest seventy-nine years. The number of cases in the various decades is as follows:

Decade	20-30	30-40	40-50	50-60	60-70	70-80
	5	25	32	27	15	3

Thus it is seen that the largest number of cases is in the decade, 40-50.

Interval from Primary Infection to Death.—The shortest interval elapsing from the primary infection to death was five years, the longest forty-eight years, with an average of about twenty years.

An effort was made to ascertain the length of time that free aortic regurgitation was present before the signs of myocardial failure appeared. This was admittedly difficult because the vast majority of our patients did not seek medical attention until signs of heart failure developed. In this series the longest interval that free aortic regurgitation was known to exist prior to the development of heart failure was six years. This was in a female whose insufficiency was due to ring dilatation with very slight involvement of the aortic leaflets. I have

*From the Medical Clinic of Western Reserve University at Cleveland City Hospital.

seen one patient whose insufficiency existed for at least eighteen years before death from heart failure.

Subjective Symptoms.—The first symptoms complained of by the vast majority of patients in this series were those of beginning heart failure—dyspnea on exertion, palpitation, and edema of the lower extremities. Precordial and substernal pain or anginal attacks were seldom noted except in those cases of marked narrowing of the coronary arteries. Even in the presence of marked constriction of the coronary mouths, chest pain was not always present. For example, in one instance of complete occlusion of both coronaries from syphilitic changes in the sinuses of Valsalva, pain was not present during the three weeks that the patient was under observation before death.

Objective Findings in the Absence of Congestive Failure.—In the majority of instances there were the well-known peripheral vascular signs of free aortic regurgitation; a thickened left ventricle with a forcible localized apical thrust, usually displaced downward and outward. More often than not a to-and-fro murmur was present, loudest over the anatomical site of the aortic orifice, but distinctly audible over the base and in the aortic area to the right of the sternum. Of the more unusual physical signs, there were two cases in this series in which the diastolic murmur was so loud as to be heard as a buzzing sound by the unaided ear several feet from the patient's bed. There was also in these two cases a marked diastolic thrill palpable over the base of the heart. In four cases a palpable systolic thrill was present, suggesting aortic stenosis, but in none of these was the aortic orifice narrowed at autopsy. In approximately 5 per cent of this series one heard over the aortic area a snappy second sound of valve closure, followed by a blowing diastolic murmur. This proved to be a valuable diagnostic sign of ring dilatation.

Objective Findings in the Presence of Congestive Failure.—In 99 cases in this series, varying grades of congestive heart failure were present at the time of death. With advancing failure the apical thrust usually became less sharply localized, and palpation over the apex revealed a more diffuse and less forcible left ventricle. At this stage the murmurs arising at the aortic orifice became less intense, and the pulse lost its characteristic water-hammer qualities. The cardiac mechanism remained normal in all but five cases. There were three instances of auricular fibrillation and two of paroxysmal auricular tachycardia. I have no accurate data on the incidence of periodic breathing in this group dying of heart failure, but certain it is that the majority had Cheyne-Stokes respiration for varying intervals preceding death.

Clinical Course.—An attempt was made to ascertain the duration of life after the onset of symptoms, but accurate information on this point was not possible in all cases. The longest interval noted was six

years, the shortest two weeks, with an average of about one year. To arrive at this average, I assumed that an individual occupied as a laborer possesses a certain myocardial reserve to permit him to carry on. If he is forced to stop work because of respiratory distress and in spite of treatment succumbs to his disease in less than a year, we are justified in including such a case in the group that died less than a year after the onset of symptoms.

The more or less abrupt appearance of cardiac symptoms, and the progressive nature of the heart failure characterized the clinical picture. For example, the following account covers the salient features observed in the clinical course of this group of patients: A well-developed male in the prime of life, with a negative cardiac history, always able to do manual labor, observes breathlessness on exertion and palpitation of the heart. These symptoms gradually increase in severity until he is no longer able to work. Edema of the lower extremities appears. At this stage he is admitted to the hospital, and one finds the cardinal signs of congestive failure: an enlarged and overactive left ventricle, with aortic insufficiency. In spite of treatment the patient may progress rapidly to death, or he may make a temporary recovery only to fail again in a few weeks or months. Certain it is that in the type of patient here considered a frank cardiac decompensation marks the beginning of the end. The majority died in less than a year from the onset of congestive failure, and it was the exceptional case that lived more than two years.

SUMMARY

Following are the conclusions reached from the clinical observations on 107 autopsied cases of syphilitic aortic insufficiency. It is probable that the type of patient included in this group—individuals from the working class, and the majority negroes—has some influence on the facts observed, though to what extent it is obviously difficult to determine.

1. Syphilitic involvement of the aortic orifice may appear as early as five years and as late as forty-eight years after the primary infection. The average time interval is around twenty years.

2. Free aortic regurgitation appearing out of a clear sky in an adult with a negative cardiac history, and with no evidence of acute infection, should be regarded as syphilis until proved otherwise.

3. Substernal pain and anginal attacks are not important symptoms in the type of cases here considered.

4. Syphilitic aortic insufficiency is more common in the negro than in the white.

5. The appearance of congestive heart failure in a patient with syphilitic aortic insufficiency is a grave omen.

DISCUSSION

Dr. F. N. Wilson, Ann Arbor, Mich.—Dr. Scott spoke of the cardiac pain which some of his patients had. He stated that in his series of cases it was relatively rare and occurred in cases in which the mouths of the coronary arteries were narrowed, and I presume that the pain was of the type referred to as angina pectoris. I have seen a few patients with syphilitic aortitis who complained of chest pain which appeared to be of a different kind. I would not venture to say that the type of pain which they had was characteristic. I remember two of these patients well; both had slight aortic insufficiency, a faint murmur without vascular signs, and slight dilatation of the first part of the aorta. The Wassermann was positive in both. They complained of a burning pain which was felt in the epigastrium or beneath the ensiform and radiated upward under the sternum. There was no radiation to other parts of the chest or to the arms. The pain was not closely related to exercise and was not relieved by nitroglycerin. Antiluetic treatment had no definite effect upon the pain while the patients were under observation. The pain was quite different from that ordinarily seen in coronary disease and this suggested that it might be the direct result of the aortic involvement.

Dr. Emanuel Libman, New York, N. Y.—I will speak briefly on the subject of the sensitiveness to pain in the patient, which is important in this type of case. In the hyposensitive type of patient we may get contralateral radiation, or radiation toward the focus (inverse radiation). There may be very marked weakness instead of pain. That is a very important point. Reflex disturbance may largely replace pain. There may be aerophagia. A patient with coronary thrombosis may have this latter symptom with dyspnea. If Dr. Wilson's patient was hyposensitive, the pain might have radiated toward the heart, instead of outward. I agree with Dr. Wilson, I have not seen very much aortic syphilis.

Dr. Smith, Iowa City, Iowa.—I would like to know if Dr. Scott thinks involvement of the coronaries as important as aortic regurgitation.

Dr. Alexander Lambert, New York, N. Y.—Why does Dr. Scott say that the ring is dilated when the valve snaps hard and there is a blowing diastolic murmur? Is that not an evidence of the valve closing with thickened edges rather than of dilatation of the ring?

Dr. Saul.—I would like to ask Dr. Scott if he encountered any cases of nocturnal dyspnea. One-third of these cases will complain of difficulty in breathing at night. They begin with nightmares, advancing to real cardiac asthma attacks. If we bear that in mind, we can advance the period of symptoms six months. This precedes dyspnea on exertion and substernal pain.

Dr. W. H. Robey, Boston, Mass.—We had an interesting case at the Boston City Hospital. A colored washerwoman of thirty-four years who had to climb three flights of stairs to her tenement, came to the ward complaining of myocardial insufficiency. She had no pain. At autopsy both coronaries were found occluded, yet she had been climbing those stairs carrying the washing for six months with that condition.

Dr. Lewis A. Conner, New York, N. Y.—This is a very accurate description of a moderately progressive case of luetic aortitis after the advent of aortic insufficiency, and it is all the more striking when one contrasts it with the benign course of uncomplicated aortic insufficiency of rheumatic origin. That is the lesson to be drawn. These cases go downhill with rapidity and certainty. On the other hand, rheumatic patients live many years and often fill out their normal span of life.

Dr. James B. Herrick, Chicago, Ill.—In cases of syphilitic aortitis with aortic regurgitation, it is not necessarily true that there must be a rapid decline. I have seen two or three patients with syphilitic aortic regurgitation who lived for several

years; one patient lasted nine years then passed out of my observation. I agree with Dr. Wilson and Dr. Libman as to pain in this type of disease. It is not always typically anginal. I have seen pain corresponding to angina, but I have also seen patients who describe a burning, or discomfort, or gnawing sensation, which was not necessarily brought on by exertion. There are many forms of bizarre precordial distress. In regard to the sharply accented aortic second sound, it has a bell-like ringing quality, somewhat different from the sound of essential hypertension of atheroma. Why, I do not know. It is not always present, but when it is it suggests syphilitic aortitis.

Dr. R. W. Scott (closing).—In reply to Dr. Lambert's question concerning the snappy valve closure sound followed by a blowing diastolic murmur as evidence of ring dilatation, I will say that these physical signs occurred in several cases which at autopsy showed a dilated aortic ring with fairly normal valve cusps. In such instances the valves may be actually larger than normal. They are approximated during diastole, causing a snappy and sometimes a tympanitic sound, but being unable to seal the dilated orifice, a regurgitant stream of blood flows back into the left ventricle, causing a murmur. It is admittedly difficult to estimate the amount of leak that may occur at the site of widened commissures. Being at the periphery of the stream, it seems likely that less blood would regurgitate through widened commissures than through a defect in the center from insufficient valve surface.

Anginal pain and nocturnal dyspnea were seldom noted in this group of patients. On the other hand, these symptoms are known to occur in some cases of syphilitic aortitis. It seems likely that the nervous organization of the patient—the susceptibility to pain—is an important factor determining the presence or absence of pain in uncomplicated syphilitic aortitis.

I have seen three cases similar to those mentioned by Dr. Robey. Both coronary arteries were completely occluded from syphilitic involvement of the sinuses of Valsalva, without infarction of the myocardium. The long time interval mentioned by Dr. Herrick did not occur in this series so far as we could determine. We have no data on the duration of free aortic regurgitation preceding the appearance of myocardial failure, but certain it is that once congestive failure appears, the prognosis in the majority of cases is bad. Therapeutic measures may lead to temporary improvement, but in our experience a frank cardiac decompensation in a patient with syphilitic aortic insufficiency marks the beginning of the end.

THE DIAGNOSIS OF CARDIOVASCULAR SYPHILIS; ANALYSIS OF CLINICAL AND POST-MORTEM FINDINGS*

WILLIAM D. REID, M.D.
BOSTON, MASS.

SYPHILITIC lesions of the aorta were disclosed in 3.5 per cent of 1678 consecutive necropsies.[1] In 79.5 per cent of these cases the disease was advanced and in most was listed by the pathologist as the primary cause of death. In a later series[2] of 100 necropsies cardiovascular syphilis was found in 7 per cent. These studies of clinical records and examination of the literature showed cardiovascular syphilis to represent 11 to 25 per cent of all organic disease of the heart.

Syphilis of the heart and aorta, after a latent period of varying length, tends to become a progressive disease; it maims and kills those in the prime of life. There is evidence that if the disease be treated adequately at an early stage its disastrous effects often may be prevented. It should, therefore, be evident that the morbidity and mortality from cardiovascular syphilis are in certain respects a reproach to the medical profession.

Greater accuracy in the diagnosis of the disease is much needed. It is the purpose of this article to discuss the symptoms and signs, introducing as far as is pertinent statistics obtained from cases proved by necropsy.

MATERIAL

The data have been obtained from various sources. A group of 61 clinical cases[3] and another of 54 necropsies,[1] both at the Massachusetts General Hospital, have been reported. A new series of 24 necropsies at the Boston City Hospital has been added. The analysis of this latter series was made particularly for this article. For this reason certain of the statistics can be drawn from the final group only, whereas

TABLE I

MATERIAL

Cases		78
	Lesions, advanced	67.9 per cent
	Lesions, moderate	26.6 per cent
	Lesions, slight	5.1 per cent
Average age		47.9 years
Males		82.1 per cent
Females		17.9 per cent
Associated with nonsyphilitic heart disease		43.6 per cent

*From the Evans Memorial and Boston University, School of Medicine.

others are obtainable from the entire series of 78 necropsies. The literature on the subject has been utilized* and in addition an unknown number of cases personally examined in hospital and private practice.

Age and Stage.—The average age in the 78 necropsy cases was 47.9 years. The lesions were advanced† in 53 with an average age of 52.5 years, moderate in 21 with an average age at death of 49.6 years, and slight in 4, whose average age was 37.7 years. The minimal age was thirty-one, eighteen, and twenty-one years, in the advanced, moderate, and slight groups, respectively. But 15 of the 78 necropsy cases achieved the age of sixty years; only two passed the age of seventy. In one of the latter the syphilitic lesions were slight and in the other moderate in degree.

Sex.—There were but 14 women in the 78 cases coming to necropsy.

Association With Other Cardiac Diseases.—These 78 necropsies of patients with cardiovascular syphilis showed additional lesions of non-syphilitic origin in 34 (43.6 per cent) of the cases. The data obtained from the final group of 24 necropsies are given in Table I. The combination of other forms of heart disease with that due to syphilis is doubtless well known. It has been pointed out[4] that its presence should always be suspected in cardiovascular disease, as antisyphilitic therapy may sometimes transform the clinical picture in a favorable direction.

SYMPTOMS

Cardiovascular syphilis often exists in the absence of symptoms. It has been said that the disease is often symptomless until complications such as aortic insufficiency or aneurysm, are present. In the out-patient group substernal pain or shortness of breath was present in all, but in about one-quarter of the necropsy cases there were no symptoms of the disease. The latter statement is, of course, the more important, as it is not surprising that the diagnosis in the living patient is usually made in patients exhibiting symptoms which draw attention to the disease.

Pain, shortness of breath, cough, hoarseness, and weakness are the more prominent symptoms. In many cases the symptomatology is simply that of congestive failure of the heart, or broken compensation if the older term is preferred. These symptoms will bear individual presentation.

Pain.—If there are symptoms, pain is prominent. It varies from an ill-defined pain in the chest, or epigastrium, or a sensation of tightness or burning about the upper sternum to the utter torture of severe angina pectoris. It may come in attacks, be associated with exertion, or be

*More fully in reference 1.

†The lesions were deemed to be slight when but a few plaques were present, moderate when there were many placques or the latter were large, and severe when the aorta was extensively involved or aortic insufficiency or an aneurysm or both were present.

present almost continuously. In location and radiation the pain sometimes resembles that of angina pectoris.

Pain was present in 28 per cent of the necropsy cases; it conformed to the syndrome of angina pectoris in but 4 per cent. Levine[5] attributed to syphilis but 7 per cent of a series of cases of angina pectoris. It is probable that the frequency of syphilis as a cause of angina pectoris has been overstressed. I would not, however, belittle the importance of syphilis as a cause of some cases of the anginal syndrome, since recognition of this etiological factor leads to therapy that is often very effective in relief of the patient from this dread affliction.

It is known that syphilis of the aorta may involve the orifices of the coronary arteries, and it is sometimes stated that this localization of the aortic lesions may account for the occurrence of angina pectoris. In our series of 78 necropsies the orifices of the coronaries were narrowed in ten cases. The right orifice was completely occluded in three instances, the left in one, and both in one. Pain, however, was recorded in but two of the patients, in each of whom the necropsy disclosed a narrowing but not complete occlusion of the orifice of the right coronary vessel. The pain did not conform to the syndrome of angina pectoris.

The relation of the pain to the condition of the coronary arteries, aside from their orifices, was carefully analyzed in the final group of 24 necropsies. In 14 cases the coronaries were normal and in 6 of these pain was present; in one it was described as a sensation of pressure, in one that of angina pectoris, and in the other 4 it was a definite pain which did not conform to the syndrome of angina pectoris. In another 6 cases there was slight to marked sclerosis of the coronary arteries but pain was absent. In the remaining 4 with slight to marked coronary lesions pain was present. It is evident that the condition of the coronary arteries was not the determining factor in the presence of the pain.

TABLE II

ASSOCIATION WITH OTHER CARDIAC DISEASE; TWENTY-FOUR NECROPSIES

Arteriosclerosis		6
Hypertensive heart disease		3
Bacterial heart disease		3
Rheumatic heart disease		4
Definite	2	
Probable	1	
Combined	1	
Terminal endocarditis		1
Congenital heart disease and arteriosclerosis		1
Rheumatic heart disease, arteriosclerosis, and hypertensive heart disease		1
Total		17*
No other cardiac disease		7

*Two cases are entered under two headings; hence the total is 17 not 19.

Further analysis disclosed that the symptom of pain was not related to the degree of syphilitic change in the aorta. In the 78 necrop-

sies there were 18 aneurysms, which gives a percentage of 23. Eleven or over half, were without pain. Fourteen of the aneurysms involved the ascending or transverse part of the arch of the aorta. The fifteenth was a small aneurysm of the descending thoracic arch. The remaining three were below the diaphragm, one each located in the abdominal aorta, the celiac axis, and the superior mesenteric artery.

Shortness of Breath.—This is a common symptom but often is not present until a few weeks or months before death. It appears to be a symptom of congestive failure of the heart and is often associated with edema of the extremities. It was noted in all but 3 of the final group of 24 necropsies. In 2 of these it was characterized as nocturnal dyspnea.

The duration of the shortness of breath in these 21 patients before entrance to the hospital was: three months or less in 4; four to eight months in 6; nine months to two years in 4; few years in 2; and unknown in 5 patients, respectively. All died after relatively short periods in the hospital. This discloses that in 10 cases, or nearly half of those affected by shortness of breath, this complaint had been present not more than eight months before their admission to the wards, and death usually followed within one to two months more.

Cough.—Only 9 of the 24 had cough, and in but 2 of these was it severe.

Weakness.—Two patients complained of weakness. It is reasonable to assume that it was present in many toward the terminal stage but was overshadowed by the other symptoms.

Hoarseness.—This symptom was noted in but one of the 24 cases. In this patient there was an aneurysm of the arch of the aorta. Hoarseness or brassy cough was not noted in 6 other patients in whom an aneurysm of the transverse portion of the aortic arch was found at necropsy.

Dysphagia may be present when an aneurysmal change in the aorta, especially the descending thoracic portion, presses upon the esophagus. It did not occur in this series.

Fever.—An irregular fever has been reported in the literature. It is of exceptional occurrence; fever was not present in any of the 78 necropsy cases that could not readily be explained by other conditions found at the post-mortem examination. I am not aware that I have ever noted it in a patient affected by cardiovascular syphilis.

Duration of the Symptoms.—The relatively short duration of the symptoms before the death of the patient is impressive. In 15 of the 24 necropsies it averaged but eight and one-half months; the extremes were three weeks and two years. In six it was unknown, in the remaining three it was recorded as months, a long time, and years, re-

spectively. (Emerson, in a statistical study,[6] notes that death usually followed within two years after the development of the disabling symptoms.)

In the clinical group[3] the average duration of the symptoms before reporting for treatment was one and one-quarter years. Twelve died; 7 who received mercury and potassium iodide averaged 1.3 years under treatment, and 5 treated chiefly with arsphenamine survived an average of 3.07 years. Ten were alive at the time of the analysis; 9 of these received arsenical therapy. Six of the latter were free of symptoms and able to work. The remainder could not be traced. The conclusion was drawn from these clinical cases that cardiovascular syphilis is a progressive disease but can sometimes be checked by adequate therapy. This opinion finds confirmation in the literature.

Manner of Death.—Patients with cardiovascular syphilis commonly die from progressive failure of the heart. In the final group of 24 necropsies 19 died of congestive heart failure; three of these died suddenly and a fourth while in sleep.

TABLE III

SYMPTOMS

Absent	25.0 per cent
Pain	28.0 per cent
Angina pectoris	4.0 per cent
Involvement of mouths of coronary arteries	12.0 per cent
With angina†	0 per cent
With non-anginal pain†	20.0 per cent
Coronaries normal*	58.3 per cent
Pain present†	42.8 per cent
Angina pectoris†	7.1 per cent
Coronaries sclerosed*	41.7 per cent
Pain present†	40.0 per cent
Aneurysm of aorta	23.0 per cent
Pain present†	38.8 per cent
Shortness of breath*	87.5 per cent
Nocturnal dyspnea†	9.5 per cent
Cough*	37.5 per cent
Weakness*	+8.3 per cent
Hoarseness*	4.1 per cent
Dysphagia	0
Fever	0
Duration of symptoms*	8.5 months
Manner of death	
From congestive failure*	79.1 per cent
Sudden*	12.5 per cent

*Percentage applies only to final group of 24 necropsies.
†Percentage applies to topic below which this item is indebted.

PHYSICAL SIGNS

The evidence of cardiovascular syphilis detected by physical examination varies according to the nature and extent of the lesions present. In many cases, before the condition has become advanced, physical examination discloses no significant abnormal signs.

Cardiac Enlargement.—The heart may be enlarged, but, as is well known, this is not always detected with accuracy by physical examination. The average weight of the heart in the series of twenty-four necropsies was 555 grams (the normal weight of an adult heart varies from 240 to 360 grams[7]). In twelve cases with an average weight of 554 grams the enlargement was detected, but in the remaining twelve with an average weight of 557 gm. the increase in weight of the organ was not disclosed by physical examination. This result is but confirmation of the fact noted above, that hypertrophy of the heart is not accurately detected by physical examination.

Supracardiac Findings.—Percussion over the great vessels, a part of the physical examination that is too frequently neglected, often discloses an abnormal area of dullness. The supracardiac dullness is most marked in the midmanubrial region and in contrast to that found in arteriosclerosis tends to extend farther to the right than the left. Simple dilatation of the ascending aorta, aneurysm, and nonsyphilitic changes must be differentiated.[8] This datum was not recorded sufficiently frequently in the necropsy series to warrant statistical analysis.

Visible throbbing of the carotids and in the suprasternal notch was present in all but 5 of the 16 cases showing insufficiency of the aortic valve.

A friction sound over the base of the heart was not observed in this series. This finding is of exceptional occurrence; I can recall its detection in but a few cases. It has been explained as due to a plastic exudate on the outer surface of the aorta, but such exudate is rarely found. Perhaps it may be present in association with certain aneurysms of the first part of the aorta.

Murmurs.—A systolic murmur was noted in 18 out of the group of 24 necropsies. It was audible over the precordia in 12, at the base in 3, at the apex in 3, and was transmitted to the neck in 3. The systolic murmur varies from faint and soft to loud and rough. Occasionally the systolic murmur at the base is accompanied by a thrill, which does not, however, indicate actual stenosis of the aortic valve.

It is well known, of course, that a systolic murmur is present in many hearts that are not affected by syphilitic or any other type of cardiac disease. When these systolic murmurs are attributed to the presence of cardiovascular lues, that at the apex is believed to be due to relative insufficiency of the mitral valve, i.e., the valvular cusps are normal but the ring of supporting muscle has dilated with the dilatation of the left ventricle so that the mitral valve does not completely close.

The aortic valve was normal in 11 of the group of 24 necropsies, but in 6 of these a systolic murmur had been present over the base of the heart. The remaining 13 cases showed some structural lesion of the valve, but in three no basal murmur was detected in life. In 4 of the 10 cases with alteration of the aortic valve and a basal murmur the valve showed

changes (such as a congenital malformation, stenosis of nonsyphilitic origin, etc.) other than mere roughening to account for the murmur. Study of these cases to determine if the basal murmur could be related to roughness of the aortic valve disclosed that such relation was very dubious.

Much attention has been directed to the systolic murmur at the base. This murmur is commonly attributed to roughening of the aortic valve but this explanation is erroneous, since it has been shown elsewhere[9] that the factor of roughness alone has little if any influence in the causation of a murmur. The more reasonable explanation is that the dilatation of the first part of the aorta, which is common in cardiovascular syphilis, causes the blood ejected through the aortic valve to form a *veine fluide* or jet. The production of a jet in the circulatory system is the most important condition causing a murmur. The physical conditions present when the vessel is dilated just beyond the unnarrowed aortic valve are identical in their effect on the column of blood ejected to those present when actual stenosis exists; both cause the *veine fluide* or jet and this the murmur. A murmur so produced is commonly transmitted best in the direction of the blood stream. My own experience in examining patients affected by cardiovascular syphilis leads me to believe that the systolic murmur at the aortic area is more frequently transmitted to or toward the neck than was recorded in the necropsy group analyzed in this report.

The diastolic murmur of aortic insufficiency is common. It was noted in 37, or 47.4 per cent, of the 78 necropsies. This murmur is of maximal audibility along the left sternal margin at the third and fourth costal cartilage, or over the second right costal cartilage. It may be audible over the entire precordia, or at times it fades away between the sternum and apex where it may again reappear, especially external to the apex. The diastolic murmur of aortic insufficiency was detected in 16 of the final group of 24 necropsies. Its point of maximal audibility was equally divided between the aortic area (second right costal cartilage) and the left sternal margin. It was transmitted to the apex in 8 cases, and to the neck in but one.

The diastolic murmur of aortic insufficiency, often present in cardiovascular syphilis, begins with the second heart sound and continues a variable period after it. In this respect it differs from the only other common murmur occurring in diastole, i.e., that of mitral stenosis; the latter never begins until just after the second sound.[10] This is in accord with the physiology of the heart since the mitral valve does not open to permit the blood to move through the mitral valve from the left auricle until just after the second sound. It is my impression that too little use is made of noting the exact time when the diastolic murmur begins. The aortic diastolic is also steadier or less rolling in quality, higher pitched, and often louder than that due to mitral stenosis.

It is generally true that diastolic murmurs do not tend to appear and disappear as do many murmurs associated with systole. However, in early cases I have noted, as pointed out by Allbutt,[11] that there may for a time be a remarkable intermittency in the murmur; later it becomes permanent.

The diastolic murmur of aortic insufficiency is sometimes audible only if the auscultation is painstakingly performed. The most favorable time is immediately following full expiration and with the patient in the erect or leaning forward posture, as was emphasized by Pardee.[12] Sometimes exercise may intensify the murmur. It occasionally happens that those who do not use the large diaphragm chest-piece of the Bowles stethoscope will detect the aortic diastolic murmur only by listening with the ear applied directly to the chest.

The relation of the diastolic murmur to the lesions of the aortic valve disclosed at necropsy is of interest. An aortic diastolic murmur was detected, as stated above, in 37 of the 78 cases herein analyzed, which gives a percentage of 47.4. The base of the aortic cusps was adherent to the contiguous part of the wall of the aorta in 9 cases, but insufficiency of the valve was demonstrable post-mortem in but 4 of these, though it was manifest in 20 other necropsies without this type of lesion. Aortic insufficiency was present clinically in all 9 of the cases with adherent cusps and in 28 others. Thus, in this series post-mortem evidence of aortic insufficiency was demonstrable in but two-thirds of the cases in which it was noted in life, and in approximately three-fourths of the cases the lesions of the cusps were not the cause of the insufficiency of the valve. Therefore, it seems reasonable to conclude that in most cases the regurgitation is mainly due to yielding of the surrounding muscle and dilatation of the aortic ring.

It is of interest that in a series of 10 necropsies, Juster and Pardee[13] found involvement of the coronary orifices in each of the 4 cases that showed aortic insufficiency, and not in the remaining 6 without the valvular insufficiency. That this combination is not constant is evident from the fact that in the series of necropsies herein analyzed there were 37 cases in which aortic insufficiency was recognized clinically, 24 in which it was evident at the necropsy, and but 10 in which there was involvement of the coronary orifices. My notes are not sufficiently complete to answer the question of whether the coronary openings ever are narrowed in the absence of aortic insufficiency, but I suspect that such may at times occur.

Austin Flint Findings at the Apex.—In well-marked cases of aortic insufficiency there are sometimes auscultatory findings at the apex which simulate those found in organic stenosis of the mitral valve. It is impossible to analyze their frequency from the data recorded in this series of cases. My personal experience in examining similar cases gives

ground for the opinion that the Flint findings are occasionally present with high grade aortic regurgitation.

Aortic Second Sound.—In the latter group of 24 necropsies there are 6 of the 16 showing aortic insufficiency in which the record contains definite statements in regard to the aortic second sound. In two of these six the aortic second sound was recorded as accentuated and the valve was normal at necropsy; in three it was masked by the murmur, and there were lesions involving the cusps. In the sixth case the aortic second was normal and the cusps were thickened, more so, in fact, than in one in which the sound was masked. This confirms the opinion that the second sound sometimes is present in spite of the insufficiency of the aortic valve. In 5 of the 24 necropsies the accentuation of the aortic second sound was noted, and as already stated, in two it was associated with the diastolic murmur of regurgitation.

Allbutt[11] emphasized a change in the quality of the second sound, the detection of which he believed to be of value in the diagnosis of syphilitic disease of the aorta. He describes it as a "tympanic second sound" and cites Potain's comparison of it to the sound of the tabourka, an Algerian drum made of an earthen pot with a skin stretched over its mouth. I am satisfied that I have at times detected such a quality in the second aortic sound, but so similar a sound may be heard in arteriosclerosis that, on the basis of the sound alone, I would not have the confidence to diagnose which of these conditions was present. It is probable that the changes in the wall of the aorta when affected by either syphilis or arteriosclerosis are sufficiently alike to have a similar physical effect on the sound produced when the aortic wall is set in vibration. When this tympanic quality of the aortic second sound is considered with all the other evidence, it may be possible to correlate it to cardiovascular syphilis or arteriosclerosis, as the case may be. This physical sign appears to be one of the minor findings and should be used circumspectly until one has acquired sufficient experience in diagnoses confirmed by necropsies, to use it successfully; probably but few have had this experience.

Corrigan Pulse.—The collapsing or water-hammer pulse was present in 11 of the 16 cases of aortic insufficiency in the final series. This vascular phenomenon was described as slight in one case, in three as moderate, and marked in the remaining seven. Its absence in the record of almost one-third of the 6 cases of aortic insufficiency is worthy of emphasis; Stewart[14] reported its absence in 48 per cent of 50 cases. In my experience many physicians are not aware of the fact that the Corrigan type of pulse is not always present in cases of aortic insufficiency. The presence of the Corrigan pulse in these cases could not be closely related to the presence or absence of lesions of the aortic cusps.

Blood Pressure.—Contrary to the belief of some there is nothing characteristic of the blood pressure in cardiovascular syphilis, unless aortic insufficiency is present when the Corrigan pulse is often but not always found. The essential feature of this appears to be a big pulse pressure, i.e., difference between the systolic and diastolic pressure levels, and usually a diastolic pressure lower than the expected normal. The extremes of the pulse pressure with the Corrigan pulse were 70 and 149 mm. Hg.; in its absence the extremes were 30 and 85. In one case in which the Corrigan pulse was noted, the diastolic pressure was 90 mm. The systolic pressure level varied from 130 to 200 mm. with the Corrigan pulse, and 114 to 235 without it. The diastolic pressure averaged 67 mm. with and 69 mm. without the Corrigan pulse. Except for the changes in the blood pressure levels associated with insufficiency of the aortic valve, it was impossible to relate the instances of elevated pressure of the blood to the presence of cardiovascular syphilis; the presence of chronic arterial hypertension could not be excluded.

Development of the Physical Signs.—May I quote from a previous paper?[15] "My first study of a series[3] of cases of cardiovascular syphilis, in which I either examined the patients or had their medical records covering frequently a period of years, has stamped indelibly on my mind the progressive nature of this disease. Case after case first showed nothing abnormal in the cardiac findings, later a systolic murmur appeared at the aortic area, and after a period of a few months to about a year, the murmur of aortic regurgitation and often that of a mitral leak and advanced heart failure developed."

Noncardiac Signs of Syphilis.—If the physical examination is conducted with sufficient care and is complete, it is not uncommon to find evidence suggestive of syphilis. Changes in the pupils, enlargement of the epitrochlear glands, alterations in the tongue, a scar on the prepuce, anal condylomata, certain scars on the skin, sabre-shaped tibiae, altered reflexes, etc., may suggest syphilis. It is noteworthy that changes in the pupils were frequent in the series of 24 necropsies. In 7 the pupils were irregular; in 6 they were unequal; in 5 the reaction to light was sluggish; and in 3 the pupil was of the Argyll-Robertson type. The pupils were normal in but 10 of the 24 cases.

WASSERMANN REACTION

The Wassermann reaction on the blood was obtained in 42 of the necropsies. In 25 it was positive, in 7 suspicious or moderately positive, and in 10 it was negative. In percentages the figures are: 59.5 per cent, 16.6 per cent, and 23.8 per cent, respectively. The percentage of positive reactions is lower than is found in much of the literature. Twenty-three per cent of negative Wassermann reactions need cause little surprise when it is recalled that this reaction is not positive at all times in cases of proved syphilis. The difficulty is that there is too

often a tendency to doubt the diagnosis of cardiovascular syphilis because the Wassermann reaction is negative. A positive reaction supports the diagnosis, but if negative the diagnosis should remain unshaken if indicated by other evidence.

As in other conditions due to syphilis the history of having had this infection is often negative. Nine of the patients in the series of 24 necropsies admitted a chancre; an average of 25 years had elapsed since the occurrence of the chancre.

The question is sometimes raised if it is not desirable to do a lumbar puncture and obtain a Wassermann test on the spinal fluid in those cases in which the test is negative on the blood. In my opinion such a procedure is both unnecessary and places too much importance upon the Wassermann reaction. As stated above, a diagnosis of cardiovascular syphilis should not be abandoned merely because the Wassermann reaction on the blood is negative. If the data as a whole indicate the presence of cardiovascular syphilis, treatment should be administered at least to the extent of an adequate therapeutic test. If a positive reaction were obtained on the spinal fluid, this does not, of course, prove the presence of cardiovascular syphilis; syphilis of the central nervous system may be present. The diagnosis of cerebrospinal syphilis is not germane to this article.

It need hardly be said that the Kahn or Hinton modifications of the Wassermann reaction should be made use of; they will probably give a somewhat higher percentage of positive reactions if syphilis is present.

ROENTGEN RAY FINDINGS

Roentgen ray examination offers further data of value in diagnosis. It is, however, inconsistent with our knowledge of the pathology of cardiovascular syphilis to believe that in early cases evidence of its presence can be disclosed by the x-ray. How can one expect that some perivascular infiltration or a few plaques in the aortic wall can be detected by the roentgen ray? In sufficiently advanced cases, however, roentgen ray examination is very helpful, often giving the first definite evidence of the presence of cardiovascular syphilis. The radiologist failed, nevertheless, to make the correct diagnosis in five cases in this series in which the lesions were advanced. When one is familiar with the complexity of the differential diagnosis, these failures need cause no surprise.

The details of the roentgen ray findings have been well described by Holmes[16] and others and will not be repeated here.

ELECTROCARDIOGRAPHIC FINDINGS

The electrocardiogram, in my experience, does not show changes indicative of cardiovascular syphilis. The electrocardiograms taken on 50 cases[17] of early syphilis were essentially normal. Nothing distinctive

was found in the tracings taken in 34 patients[18] clinically diagnosed to have syphilitic heart disease. However, a recent study[13] of 50 patients with cardiovascular syphilis disclosed the following: the T-wave was abnormal in 85 per cent of the 16 patients having aortic insufficiency and in 20 per cent of these the T-wave was of the coronary type. In the 34 patients without the aortic leak the T-wave was abnormal in but 38 per cent, and only one case (7 per cent) showed a wave of the coronary type. The prognosis was much more unfavorable in the patients with the abnormal T-waves.

TABLE IV

SIGNS

Average weight of heart*	555 grams
Enlarged heart*	91.6 per cent
Aortic insufficiency*	
Present†	66.6 per cent
Absent†	33.3 per cent
Systolic murmur*	75.0 per cent
Diastolic murmur	47.4 per cent
Aortic cusps adherent to aortic wall†	24.3 per cent
Diastolic murmur*	66.6 per cent
Transmitted to apex†	50.0 per cent
Transmitted toward neck†	6.2 per cent
Aortic second sound*	
Accentuated	20.8 per cent
With aortic insufficiency	
Accentuated	12.5 per cent
Masked	12.5 per cent
Unmentioned	75.0 per cent
Corrigan pulse, with aortic insufficiency*	
Present	68.7 per cent
Absent	31.3 per cent
Pupils	
Abnormal	58.7 per cent
Irregular	29.2 per cent
Unequal	25.0 per cent
Sluggish	20.8 per cent
Argyll-Robertson	12.5 per cent
Wassermann reaction	42 cases
Positive†	59.5 per cent
Suspicious†	16.6 per cent
Negative†	23.8 per cent

*Percentage applies only to final group of 24 necropsies.
†Percentage applies to topic below which this item is indented.

In my opinion it seems best to consider abnormalities in the electrocardiogram to be indicative of the presence of cardiac disease, but not of the etiology of the latter. Thus, one finds electrocardiograms depicting various degrees of heart-block, bundle-branch block, auricular fibrillation, etc., in cases proved by necropsy to have cardiovascular syphilis, but the diagnosis of syphilis as the causative factor cannot be determined from the electrocardiographic findings. When these latter are correlated to the data obtained by the other methods of clinical and laboratory examination, they may be decided to be of luetic origin and contribute much to the understanding of the case.

DISCUSSION

The presence of cardiovascular syphilis was diagnosed clinically in 43 of the entire series of 78 necropsies; in 35 it was not. In 12 of the latter the lesions were of an advanced degree. There was, then, a failure to diagnose the disease in 44 per cent, and in 34 per cent of these failures the condition was in an advanced state.

The first essential in the diagnosis of cardiovascular syphilis is that it be considered as one of the possible diagnoses in any adult in whom cardiac disease is deemed to be present. The more or less recent recognition of the necessity of determining the type of heart disase, i.e., rheumatic, hypertensive, syphilitic, etc., is proving of value in the detection of those cases in which cardiovascular syphilis exists. The modern clinician is no longer satisfied with the diagnosis of myocarditis as a complete statement of the condition that may be present; some of these are instances of cardiovascular syphilis in which the myocardial changes are but one feature.

Every case affected by syphilis is one of potential heart disease.[19] The term potential heart disease is applicable here as it is in those who have had one of the rheumatic group of infections, such as rheumatic fever, chorea, or tonsillitis. The interval between the primary stage of syphilis and the onset of clinical disease of the heart and aorta is, of course, much longer than that usually elapsing in the case of rheumatic heart disease.

DIFFERENTIAL DIAGNOSIS

The presence of cardiovascular syphilis is the more probable if other conditions can be excluded as the cause of the abnormal symptoms and signs pertaining to the circulation. Such conditions as nonspecific aortitis, arteriosclerosis of senescence, hypertensive heart disease, rheumatic heart disease, pulmonary tuberculosis, mediastinal tumors, and perhaps some cases of tabes dorsalis are among the more significant diseases from which cardiovascular syphilis must be differentiated. The details of differential diagnosis have been sufficiently discussed elsewhere.[1, 8, 16, 20]

SUMMARY

The symptoms and signs of cardiovascular syphilis are discussed. An analysis was made of 61 clinical cases and 78 necropsies; statistics limited to the cases proved post-mortem are presented.

The average age at death was 47.9 years. There were but 3 cases under thirty years of age, and only 2 above seventy years.

Males outnumbered the females in the ratio of 5.5 to 1.

The syphilitic lesions were associated with lesions of nonsyphilitic disease of the heart in 43 per cent of the necropsies.

Symptoms of the disease were absent in about one-quarter of the patients in whom the disease was disclosed at necropsy.

Pain was present in 28 per cent. It conformed to the syndrome of angina pectoris in but 4 per cent.

The mouths of the coronary arteries were partially occluded in 10 patients; none of these had angina pectoris, and 8 were without pain of any sort.

Neither the presence nor the character of the pain could be related to the condition of the coronary arteries or of the aorta.

The coronary arteries were normal in 58.3 per cent of the series of 24 necropsies.

Shortness of breath was common after the onset of congestive failure of the heart.

The symptoms of weakness, hoarseness, dysphagia, and fever were absent or were present in a negligible number of these patients. Hoarseness of the voice was noted in but one of seven cases of aneurysm involving the transverse portion of the aortic arch.

The duration of the symptoms rarely exceeded a few months in the necropsy cases; it was somewhat longer in the clinical series treated as out-patients. From these latter there is presumptive evidence that adequate therapy may relieve symptoms and prolong life.

The manner of death was that of progressive failure of the heart in 79 per cent of the series of 24 necropsies. In 4 of these the actual death was sudden.

The heart was enlarged in 22 cases, or 91.6 per cent, of the 24 necropsies. This enlargement was present in the absence of aortic insufficiency in 7, or about one-third of the group. The average weight of the heart was 555 gm.

Increase in the supracardiac dulness and other findings above the heart are common, but too often not recorded in the physical examination.

A systolic murmur over the precordia or more localized at the apex or base is common. That at the base is not due to roughening of the aortic valve.

The diastolic murmur of aortic insufficiency was noted in 47.4 per cent. In 50 per cent of the 16 aortic regurgitant cases in the series of 24 necropsies the diastolic murmur was transmitted to the apex.

This diastolic murmur may be inconstant in its presence in its earlier stages. Its detection sometimes requires painstaking auscultation.

Aortic insufficiency was recognizable in half again as many cases as were evident at post-mortem, and in at least three-fourths of the cases (murmur present in life) the regurgitation could not be attributed to lesions of the valve. The insufficiency of the valve is best explained as due to yielding of the muscular ring round the aortic orifice.

The apical findings, known as those of Austin Flint, are occasionally present.

The aortic second sound may be masked by the murmur of aortic insufficiency, or it may be accentuated in the absence of the murmur and even if the latter is present.

A change in the quality (i.e., a tympanic note) may take place in the aortic second sound, but it is difficult to differentiate from that found in arteriosclerosis of nonsyphilitic causation.

The Corrigan type of pulse was absent in 5 of 16 cases of aortic insufficiency. That such is possible does not appear to be generally recognized.

There is nothing characteristic of the blood pressure save in the presence of aortic insufficiency.

Careful physical examination may detect evidence suggestive of syphilis elsewhere in the body.

The Wassermann reaction was negative in 10, or 23.87 per cent, of the 42 cases in which it was recorded.

The roentgen ray findings are very important aids in the diagnosis. It is unreasonable, however, to expect that the slight lesions in early cases of cardiovascular syphilis can be detected by the roentgen ray. In advanced cases the differential diagnosis from nonsyphilitic conditions may be difficult or impossible solely from the roentgen ray findings.

The presence of cardiovascular syphilis was not diagnosed in 44 per cent of this series, although the subsequent necropsy disclosed advanced lesions in one-third of these failures.

About one in five of the cases in which the syphilitic lesions were of advanced degree remained undiagnosed in life.

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DISCUSSION

Dr. Alexander Lambert, New York, N. Y.—I would like to ask Dr. Reid to explain his differentiation of pain of the coronary type and the noncoronary type in syphilitic disease. Pain in coronary disease is known to be three and one-half times as frequent in the hypochondria and epigastrium as in the chest and down the left arm.

Dr. Wm. D. Reid (closing).—If I understood Dr. Lambert rightly he asked for more details as to how we separate pain called angina pectoris from the other group. There is a large degree of the personal equation of whoever answers this question; classifications of angina differ considerably. Angina pectoris is closely related to exertion and is relieved by nitroglycerin. The pain is of short duration and has a typical radiation. In the other group the pain is not particularly under the sternum, is not related to exertion, and is of longer duration. A woman can do her housework all day without pain and have the pain at night. When the Wassermann reaction is negative, it does not mean that the cardiac condition is not due to syphilis. Dr. Hinton, of Boston, is working on a modification of the blood Wassermann which will be much more specific, and it is hoped make it unnecessary to test the spinal fluid. However, we must not rely so much on the Wassermann as on the general picture.

THE DIFFERENTIATION OF SYPHILITIC FROM FUNCTIONAL AND OTHER FORMS OF AORTIC INSUFFICIENCY*

LESLIE T. GAGER, M.D.
WASHINGTON, D. C.

IN THE degree that a disease is endemic, its diagnosis is likely to become deceptively easy. Where acute rheumatic fever prevails as the chief cause of heart disease, as in New York and New England, it is natural, in relation to aortic insufficiency, to think first of this etiologic agent. In Washington[10] and further south, as syphilis, especially in the negro,[16] comes to equal and surpass other infections in producing the cardiovascular lesions of early and middle adult life,† there results a distinct diagnostic leaning toward this disease.

Inferences based on probabilities are often correct: in spite of her age, the diagnosis of syphilitic aortitis was made in a seventeen-year-old negro girl with aortic insufficiency (there was a positive Kahn test and no rheumatic history) and confirmed at necropsy. But in other patients, in whom the diagnosis of syphilitic aortic insufficiency had been made, or seriously considered, this etiology was disproved, and some of these problems of differential diagnosis I wish to discuss and illustrate.

Under the title of true and false aortic insufficiency, Barié,[2] in 1896, presented an extensive review of the subject, much disputed since Corrigan,[6] of the differing modes of origin and meaning of diastolic murmurs arising, if not always heard, at the base of the heart; and his classification remains so useful and practical a guide that I have followed it in the accompanying schema. His views, indeed, Barié defended in 1923, when interest in functional aortic insufficiency had been renewed by a series of case reports.[3, 13, 14]

Of these five groups of possible signs or simulations of aortic insufficiency, the last four, while of much interest, must be rapidly disposed of here.

The diagnosis of aortic insufficiency without the diastolic murmur has not often been made, though frequently in hyperthyroidism and not rarely in hypertension, a high pulse pressure suggests the search for regurgitation. Dumas,[7] however, has recently reported an example, proved by necropsy, in which the recognition was based on high pulse and differential pressures and loss of the aortic second sound. The clinical observations of Fürbringer, Leyden and Litten are cited by

*From the Department of Medicine, George Washington University School of Medicine.

†Dr. Frank Leech informs me that of 3715 admissions to the Children's Hospital, Washington, D. C., in 1929, there were 46 cases of rheumatic infection and 34 cases of rheumatic heart disease (0.92 per cent). No syphilitic heart disease was found.

Barié, who quotes Leube's opinion that in advanced insufficiency the valvular alterations might be so great as to prevent the vibrations necessary to produce a murmur.

Propagation of the aortic diastolic murmur from base to apex or beyond, or to the region of the xiphoid process, dependent on predominant lesions of the posterior cusps or other factors, has become a familiar observation.

The suspicion of syphilis aroused by an accentuated, bell-like or drum-like aortic second sound (Potain's bruit de tabourka) may be heightened when a coincident whiff or short diastolic murmur is audible. But the underlying changes in the root of the aorta need not be syphilitic.[1] These signs, in a hypertensive patient with a history of chancre, aortic dilatation and a positive Wassermann reaction and a temporarily favorable response to the therapeutic trial of a few small doses of neoarsphenamine, were subsequently found to be associated with simple atheromatosis and unchanged valves. Austin Flint[9] described this "aortic diastolic non-regurgitant murmur," which is characteristically linked with a systolic aortic murmur and is entirely an arterial phenomenon.[2, 4] But a diastolic murmur may be frankly audible at the base or along the sternum, and its seat of origin be not at all clear, just as its intensity is notoriously independent of extent of lesion or amount of regurgitation.

TABLE I

CLASSIFICATION OF AORTIC INSUFFICIENCY

I. With a basal diastolic murmur.
   A. True insufficiency.
      Valve lesions due to
      1. Malformation
      2. Trauma
      3. Endocarditis
      4. Syphilis
      5. Sclerosis
   B. Functional (relative) insufficiency.
      Dilatation of aortic ring, without valve lesion.
      1. Dilatation of aorta, e.g., by hypertension.
      2. Dilatation of left ventricle: anemia, failure.
      3. External traction: adherent pericardium.

II. With accentuated aortic second sound obscuring a diastolic murmur, or coinciding or alternating with it.
   Due to atheromatous, and usually dilated, aorta.

III. With an apical diastolic murmur only (transmitted from aortic area).

IV. With no diastolic murmur audible (peripheral signs only).

V. Pseudoinsufficiency (with a diastolic murmur arising elsewhere than in the aortic area: pulmonic insufficiency [Graham Steele]; septal defect; accidental).

A man of twenty-eight years, who has had no intimation of heart disease and who denies both rheumatic and syphilitic infection, though the blood Wassermann test is four plus, has come under observation following an hemoptysis. The lungs are clear. Aortic dulness is not widened, but both to right and left the heart is greatly enlarged. Over the precordium is a long systolic thrill, and a harsh

systolic murmur is loudest in the third and fourth interspaces at the sternal border. In the same area is heard a smooth high-pitched diastolic murmur which is not made out at the base. Blood pressure is 125/60 mm. in both brachial arteries, 160/60 in the femoral. The liver is not enlarged. There is no clubbing or cyanosis of the fingers.

Is this syphilitic aortic insufficiency or a septal defect? In all diameters fluoroscopy shows an undilated aorta. The globular heart measures 17 cm. in transverse diameter, with chest width 26 cm. The electrocardiogram shows no ventricular predominance.

Pulmonic insufficiency is usually set apart by the presence of mitral stenosis and the absence of ventricular hypertrophy and peripheral signs of aortic insufficiency, but Holt[12] has shown the difficulty of differentiation that may arise. In her patient, with a large heart, mitral stenosis and terminal pneumococcus endocarditis, an adherent pericardium was found at necropsy, the same condition which Laubry and Doumer[13] found associated with dilatation of the left ventricle and relative aortic insufficiency. In such cases, the possibility exists of external traction and deformity of the aortic ring; protrusion of the septal wall into the ventricle with elevation of a cusp has been suggested,[4] while the important factor of ventricular dilatation in throwing strain on the aortic vestibule and orifice is shown by the following patient:

A negro male, aged forty-one years, was admitted to the hospital with fever and weakness. Eight weeks before admission his tongue had become covered with white patches, a blood Wassermann test was found positive and several intravenous injections were given.

In addition to an intense stomatitis, examination revealed marked carotid pulsations, a greatly enlarged heart and a blowing diastolic murmur to right and left of sternum in the second interspace. The blood pressure was 128/54 mm. The diagnosis seemed obvious until the sudden onset of hemiplegia brought up the question of bacterial endocarditis. The necropsy revealed a normal aorta and intact aortic valves; both ventricles were enormously dilated and on one mitral cusp was a large fresh vegetation. Staphylococci were recovered from the heart's blood.

Goldstein and Boas[11] have linked the functional diastolic murmur occurring in severe anemia with the presence of cardiac dilatation, and this has been my observation in two recent cases, while in a man whose hemoglobin, before liver extract was given, had dropped to 9 per cent, there was neither cardiac embarrassment nor murmur.

Inconstancy is frequently a characteristic of the functional basal diastolic murmur. An instance of its modification by change in position of the patient is of interest:

A negro male of about thirty years was admitted with the signs of tuberculous pleurisy with effusion and was tapped. Without central or peripheral evidence of circulatory disease, and a negative Wassermann test, this man showed a distinct diastolic murmur at the base of the heart while in the recumbent position. In the erect position, the murmur disappeared.

How shall such a murmur be explained? Potain noted a soft circumscribed murmur in a tuberculous patient whose aorta and valves were later found normal (cited by Barié). In such patients as these, mediastinal adhesions between aorta and chest wall are not beyond possibility. Barié considered murmurs of this description to be accidental, cardiopulmonic, possibly venous in origin, and often definitely associated with anemia.

Hypertension, both transient and persistent, bears an important causal relation to functional aortic insufficiency. The appearance of a diastolic murmur with an attack of bronchial asthma was noted by Fleckseder[8]; in Vaquez's[19] patient, a man with hypertension and angina pectoris, aortic insufficiency appeared during a severe attack of pain and disappeared with its recession.

Numerous observers[2, 3, 13, 14, 15, 19] have noted the association of aortic dilatation and relative aortic insufficiency with chronic hypertension or granular kidneys. The salient features of three such examples follow:

A male, aged thirty-two years, was sent to hospital from the heart clinic, because of fatigue and dyspnea, with blood pressure 268/178 mm. He was rather well nourished, only slightly anemic, showed a faint trace of albumin in the urine, and had a negative blood Wassermann reaction. Retinitis appeared; the urea nitrogen increased from 29 mg. to 188 mg. per 100 c.c. of blood, and death occurred in six weeks. There was constantly present a loud blowing diastolic murmur in the second right interspace and down the left border of the sternum. At necropsy, the aortic ring was distinctly dilated, and there was well-marked atheromatosis, but the valves were only slightly thickened.

A man, aged sixty-eight years, with dyspnea and pain of aortic distribution, showed moderate peripheral arteriosclerosis, a rather large heart, some dilatation of the aorta, and a blood pressure of 240/130 mm. There was a booming aortic second sound, and a high pitched murmur occupying most of diastole was heard in the second right interspace, down both sides of the sternum and also outside the apex. Post-mortem study, after rupture of a dissecting aneurysm, showed the aortic orifice dilated, with no valvular disease and only slight sclerotic changes in the intima of the aorta.

A laborer, aged thirty-nine years, recently came under observation complaining of palpitation, breathlessness and cramps in the legs. His blood pressure was 230/150 mm.; aortic and cardiac dulness was increased, and a long basal diastolic murmur was present on both sides of the sternum and transmitted down its left border. There was a history of chancre at twenty-five years, but the blood Wassermann test was negative. While syphilis was not excluded, it was felt that the high diastolic pressure was strong contrary evidence.

Of the less common causes of valvular lesions, fenestrated cusps[8] and other anomalies[17] may cause insufficiency or aid in dilatation of the ring. Rupture of a cusp following heavy lifting was seen in a young syphilitic negro, with a rough double thrill and murmur at the base. In an ex-prize fighter of thirty-four years, apparently healthy and an applicant for insurance, a fairly harsh aortic diastolic murmur was unexpectedly discovered. Rheumatic and syphilitic infections were denied, and his wife has had four healthy children. Sclerosis of the valves,

without antecedent hypertension, I believe to be rare, in spite of senescent dilatation of the aorta[5, 18] as an accessory factor.

In summary, in the course of studying aortic insufficiency and diastolic murmurs under conditions, such as race, age, sex and climate, which make syphilis the outstanding etiologic factor, exceptions have been found frequently enough to show a plurality of causes and mechanisms. Not the least interesting finding has been that of relative aortic insufficiency. Differentiation requires avoiding a diagnostic bias and giving attention to the whole clinical picture.

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DISCUSSION

Dr. F. N. Wilson, Ann Arbor, Mich.—I should like to point out that the importance of any condition depends upon its frequency. Of the cases of aortic insufficiency that I have seen, 90 per cent or more have been either rheumatic or leutic. I have seen cases of arteriosclerotic aortic insufficiency, but in my experience this condition has been relatively rare. I have never seen a case of free aortic regurgitation, that is aortic regurgitation with pronounced vascular signs, due to this cause. The percentage of all cases of aortic insufficiency due to subacute and acute bacterial endocarditis is relatively small. Congenital aortic insufficiency is very rare.

I have never seen an instance of aortic insufficiency which I could attribute with confidence to functional dilatation of the aortic ring, nor have I ever seen an accidental aortic diastolic murmur. I do not question that both occur, but I believe that they are very rare.

The great majority of the cases of aortic regurgitation in which pronounced vascular signs occur are luetic. Another sign that should lead one to suspect luetic involvement of the aorta is the presence of palpable pulsation when the fingers are placed upon the cricoid cartilage. The heart beat cannot normally be felt at this point. I believe that the change in the aortic second sound which occurs in luetic aortitis differs from that which occurs in hypertension and in arteriosclerosis, and I believe that this difference is due to the dilatation of the first part of the aorta in luetic aortitis. The arteriosclerotic aorta is lengthened rather than dilated, and the quality of the second sound is different.

Dr. Lee, Washington, D. C.—I think Dr. Wilson's remarks are well taken. The burden of proof belongs to those who have to show that it is not an organic condition. We do sometimes have functional diastolic murmurs. One old lady had an atheromatous condition with a typical long diastolic murmur after severe fits of coughing, with stress on the circulation which, however, was not present at other times. Sometimes these cases are temporary, sometimes permanent, but they are rare.

Dr. H. S. Feil, Cleveland, Ohio.—Some years ago I studied the subclavian pulse in a large series of aortic cases. Registration was made by means of the optical sphygmographic method of Wiggers. It was found that the pulse in luetic aortic insufficiency was characteristic. When ejection was free, the case was usually luctic, while with evidence of stenosis the pathological lesion was rheumatic or sclerotic.

Dr. Gager (closing).—I do not wish to leave the impression that in the majority of instances the aortic insufficiency of adults which I see in Washington is not syphilitic. But every now and then occur these exceptional cases of aortic insufficiency which, because specific aortitis is common, may be diagnosed as due to syphilis when some other condition is responsible. It is the practical importance, for prognosis and treatment, of keeping in mind and recognizing these various possibilities, as well as the interest of the differential diagnosis, that I would emphasize.

A STUDY OF THE COURSE OF SYPHILITIC CARDIOVASCULAR DISEASE*

FREDRICK A. WILLIUS, M.D.
ROCHESTER, MINN.

THIS study was undertaken to obtain data relative to the duration of life of patients with cardiovascular syphilis. I have been unable to find definite information regarding this point in the medical literature. Studies of this type are of considerable importance as they permit the substitution of relative quantitative values for uncertain clinical impressions. They may be said to represent the life cycle of disease.

MATERIAL AND METHOD

This investigation comprised 100 men selected from a group of 600 patients with cardiovascular syphilis. Cases were included in the study only if the following factors were present: (1) an accurate history of the time of onset of syphilis, (2) the presence of syphilitic cardiovascular disease, and (3) the exact date of and the mode of death from cardiovascular disease. The strict adherence to these criteria, which was necessary in order to obtain reliable data, account for the relatively small series. The patients were all males. To obtain accurate histories of the time of onset of syphilis in women is difficult. This is partly the result of their reluctance to confess that they know the time of onset and in part to the fact that there are greater possibilities of failure to recognize the existence of a primary syphilitic lesion in a woman than in a man.

The cases were grouped according to the type of lesion as determined by clinical methods of examination. The diagnosis of the type of lesion is presumed to be as accurate as clinical methods will permit. In addition to a complete general examination and routine laboratory investigation the patients were all subjected to roentgenographic study of the heart; electrocardiograms were taken of all, the Wassermann reaction of the blood was determined in all cases, and of all but six, studies of the spinal fluid were made. Detailed neurological investigation was conducted whenever it was thought necessary.

RESULTS

The cases were grouped as follows: (1) syphilitic aortitis, (2) syphilitic aortitis with aortic insufficiency, and (3) thoracic aneurysm.

Syphilitic Aortitis.—Seventeen cases comprised this group. The average age of the patients at the time that syphilis was contracted was

*Read by title from the Section on Cardiology, The Mayo Clinic, Rochester, Minn.

thirty-one years. The earliest age was nineteen years, and the latest age recorded was fifty-three years. The average age at which these patients died of cardiovascular disease was fifty-four years; that is, an average of twenty-three years elapsed from the onset of syphilis to the time of death. Seizures of cardiac pain occurred in three cases and these were the only instances in which sudden death occurred. The Wassermann reactions of the blood were positive in 65 per cent of the cases. Examinations of the spinal fluid were carried out in fourteen cases and in only two the reaction was positive. Syphilis of other systems of the body was demonstrated in 24 per cent of the cases. Important alterations in the electrocardiogram occurred in twelve cases (71 per cent). Significant T-wave negativity occurred in eleven cases. Two instances of auricular fibrillation were observed. The relatively rare association of auricular fibrillation and aortic disease has been emphasized on numerous occasions.

Syphilitic Aortitis With Aortic Insufficiency.—This group comprised fifty-nine cases which uniformly presented advanced cardiovascular involvement. The average age of occurrence of the primary syphilitic lesion in this group was twenty-six years, five years earlier than in Group I; the youngest patient was aged sixteen years and the oldest, forty-nine. Death from cardiovascular disease occurred at the average age of forty-nine years; this is an average period of twenty-three years from the inception of the syphilitic infection. Painful cardiac seizures occurred in fifteen (25 per cent) of the cases, and in eight of these death occurred suddenly. The Wassermann reactions of the blood of 68 per cent of the patients were positive. In fifty-six cases studies of the spinal fluid were made; eleven were positive. Associated syphilitic disease occurred in seventeen cases. Electrocardiographic abnormalities of importance occurred in thirty-seven cases (63 per cent). Significant T-wave negativity, as in Group I, was the predominant graphic characteristic. It occurred in thirty-three cases. There were two cases of complete heart-block, one of delayed auriculo-ventricular conduction, and one of complete right bundle-branch block. Only two cases of auricular fibrillation occurred.

Thoracic Aneurysm.—In twenty-four cases, thoracic aneurysm was present. The aortic arch and ascending aorta were involved in twenty-two cases, whereas there was aneurysm of the descending aorta in two. Patients in this group had contracted syphilis at the average age of twenty-seven years. The earliest age of infection was nineteen years and the latest, forty years. The average age at which death occurred from cardiovascular disease was fifty-three years, twenty-six years after infection. The average period of duration is comparable to those of the other groups. Painful cardiac attacks occurred in ten cases (42 per cent). Sudden death occurred in all but four cases, and in most of them it occurred presumably from rupture of the aneurysm. The high

incidence of positive Wassermann reactions of the blood occurred in this group, namely, 83 per cent. Examinations of the spinal fluid were conducted in all cases, and 25 per cent showed positive reactions. Associated syphilitic manifestations were revealed in five cases. As anticipated, the incidence of electrocardiographic abnormalities was small; only four instances (17 per cent) occurred. In four cases, significant T-wave negativity was disclosed, and delayed auriculo-ventricular conduction was found in one case.

DISCUSSION

Although the number of cases comprising this study is relatively small, the data derived from them are probably fairly reliable and representative of the course of cardiovascular syphilis.

The relatively long periods of apparent latency that occur in syphilis have been emphasized by many writers on the subject. In keeping with the observation, a relatively long average period of time elapses from the initial syphilitic infection until death occurs from cardiovascular involvement. Even though this period is relatively long, death occurs considerably earlier in life than the age at which death would be anticipated in normal persons.

It was not possible to draw any definite conclusions concerning the influence of treatment on the course of the disease. Much of this information could be derived only by inquiry, and in many of the cases it was so inaccurate and uncertain as to be of no value.

TABLE I

SUMMARY OF DATA

	CASES	AVERAGE AGE OF OCCURRENCE OF SYPHILIS, YEARS	AVERAGE AGE AT TIME OF DEATH FROM CARDIOVASCULAR DISEASE, YEARS	AVERAGE DURATION OF COURSE, YEARS
Group I, syphilitic aortitis	17	31	54	23
Group II, syphilitic aortitis with aortic insufficiency	59	26	49	23
Group III, thoracic aneurysm	24	27	53	26

THE DIAGNOSIS OF SYPHILITIC AORTITIS WITH NEGATIVE WASSERMANN REACTIONS*

SAMUEL A. LEVINE, M.D.
BOSTON, MASS.

THE clinical diagnosis of syphilitic aortitis is often difficult and sometimes impossible. This is particularly true under certain circumstances. There are three conditions which enable us either to suspect the diagnosis or at least to avoid overlooking it. These are the presence of a definite aneurysm of the aorta, made out either by physical or x-ray examination, the finding of aortic insufficiency or the presence of a positive Wassermann reaction in the blood. The occurrence of any one of these three findings should be sufficient to focus our attention on syphilis as the possible underlying factor in any cardiovascular case. The purpose of this brief review is to find how frequently the above criteria are absent in proved cases of syphilitic aortitis and to see whether there are any means available for recognizing the condition at the bedside. An analysis was, therefore, made of all the cases of syphilitic aortitis that came to autopsy at the Peter Bent Brigham Hospital. There were forty such cases available for this study.

Of the 40 proved cases of luetic aortitis 12, or 30 per cent, had negative Wassermann reactions in the blood. The number of blood tests varied from one to three and in no case was a provocative test done. All the Wassermann reactions were carried out under the same standard conditions. A few cases were considered as positive although the test at the hospital was negative, because it was known that at some previous time the test had been positive. It is clear that we must be ready to diagnose syphilitic aortitis even in the face of a negative Wassermann, for in 30 per cent of the cases the test failed to give the desired information. It is believed by some, and there is evidence to support the view, that this percentage would be further diminished if provocative tests were carried out.

As has been mentioned above, the finding of an aortic diastolic murmur indicating aortic regurgitation should direct our attention to syphilitic heart disease. This is especially true when it is found in individuals around the age of forty or over. The two other conditions in which aortic regurgitation frequently occurs are rheumatism and arteriosclerotic hypertensive heart disease. In general, it may be said that aortic insufficiency occurring in individuals under forty years of

*From the Medical Clinic of the Peter Bent Brigham Hospital, Boston.
Read by title.

age in the absence of obvious well-marked hypertension, is apt to be rheumatic in origin. There were three cases, however, thirty-eight and thirty-nine years old, in this series in which syphilitic aortitis without aortic insufficiency was present. If the series were larger, no doubt instances would have been found of comparatively young patients with luetic aortic insufficiency. The problem of distinguishing rheumatic from syphilitic aortic insufficiency becomes increasingly difficult at times because of the frequency of the negative past history of syphilis in the syphilitic cases and of a negative rheumatic history in the rheumatic cases. In this connection it is helpful to uncover evidence of stenosis of either the mitral or the aortic valves, for when such findings are made out, one may be quite certain that the condition is rheumatic and not syphilitic. There was no instance of stenosis of the mitral or aortic valves in these 40 cases and although such a case might be found, it must be a rare occurrence. There were 17 cases showing definite aortic regurgitation. This means that in somewhat more than half of our patients the syphilitic process in the aorta did not extend to the valves, which remained competent. The inference, however, may well be made that any patient forty years old or over who has aortic insufficiency and no stenosis of any of the valves should be regarded as possibly syphilitic.

The discovery of a definite aneurysm of the aorta as distinguished from a slight dilatation of the aorta so frequent in hypertension should be considered as a positive evidence of syphilis. At times the distinction between a true aneurysmal formation and a diffuse dilatation of the aorta is not simple. Careful x-ray examination is extremely valuable in making this differentiation. There were 17 cases showing evidence of aneurysm at autopsy. In only 12 of these cases was the diagnosis of aneurysm made clinically. In 7 of these 17 there was aortic regurgitation and that was sufficient to direct our attention to a syphilitic process.

A careful review of the clinical data of these cases showed that in some the diagnosis was quite evident from the findings on physical examination. In others, the history of pain in the upper chest or suffocation and cough was sufficient to direct our attention to aneurysm of the aorta as the cause of the complaint. There remained a few, however, in whom the aneurysm produced no physical signs that were detectable and no particularly characteristic symptoms. Here the x-ray examination was practically the only means of detecting the underlying condition. A more liberal use of x-ray and fluoroscopy of the aorta and a more careful roentgenological interpretation of these findings would certainly enable us to detect some cases of aneurysm of the aorta that would otherwise be overlooked.

The past history of syphilitic infection was of uncertain value in this group of patients. In only 18 was there either a definite history

of syphilis or sufficient related features to make one suspect that the patient was luetic. In this connection the finding of Argyll-Robertson pupils or characteristic changes in the spinal fluid is most important. It follows from this that in a little less than one-half of the cases, the history itself might direct our attention at a proper diagnosis, but that in the other half no such aid in the history would be obtainable. It is very questionable how much real help one obtains from the presence or absence of a past history of repeated miscarriages. There are so many nonsyphilities who have had repeated miscarriages and so many syphilities who have not.

It is interesting to analyze more intimately the 12 cases that had a negative blood Wassermann reaction. Of these there were 4 that had definite aortic insufficiency, two of which in addition had an aneurysm of the aorta, and a positive past history of syphilis. Of the other two the past history was positive in one and negative in the other. There were also 4 of these 12 who had an aneurysm of the aorta and no aortic insufficiency. Of these 4 the past history was positive in one, negative in two, and questionable in the other. There remain 4 cases of definite luetic aortitis in this series that showed no evidence of aneurysm or aortic insufficiency and had a negative past history of lues and showed a negative Wassermann reaction in the blood. This would indicate that in 10 per cent of our cases all of the above distinctive features that might direct one's attention to a luetic process were absent. (Cases 9, 30, 31, and 37.) If cases of the type of the last four are to be recognized clinically, the diagnosis will have to be made on indefinite evidence of a character that may be regarded as suspicious, or more careful interpretation of the x-ray findings in the aorta and possibly on a more liberal use of a provocative Wassermann test.

HISTORY OF CASES WITH NEGATIVE WASSERMANN

CASE 4.—A fifty-six-year-old white man died having shown signs of definite aortic regurgitation and aortic aneurysm. The aneurysm was discovered by x-ray examination. He gave a history of primary infection but the Wassermann was negative on two occasions.

CASE 9.—A forty-five-year-old white woman died of bronchial pneumonia three days after entering the hospital. There was no past history of lues and the heart examination was negative. Autopsy showed bronchial pneumonia and luetic aortitis.

CASE 11.—A fifty-three-year-old white man died having shown definite evidence of aortic insufficiency and aneurysm. There was a positive past history of lues. The Wassermann test was negative on two occasions. The autopsy showed a rupture of an aortic aneurysm into the right pulmonary artery.

CASE 15.—A sixty-one-year-old white man entered the hospital complaining of pain and swelling in the right upper quadrant, cough, and dyspnea. There was a questionable old history of lues. Examination showed an enlarged heart, a to-and-fro pericardial friction, a markedly enlarged liver, and signs of pneumonia of the right lower lobe. Autopsy showed a definite aortic aneurysm and luetic aortitis.

CASE 18.—A sixty-three-year-old Spaniard entered the hospital in delirium. There was a past history of lues. Examination of the heart was negative. There was evidence of tumor of the brain for which he was operated on and died a few days later. Autopsy showed carcinoma of the lung, metastasis to the brain, luetic aortitis, and a small aneurysm of the aorta.

CASE 20.—A thirty-year-old colored woman entered the hospital complaining of cough, weakness, nausea, vomiting, and increasing dyspnea. There was no past history of lues, although she had had two miscarriages. The heart was enlarged and there was a systolic murmur over the precordium. Wassermann was negative on two occasions. The clinical diagnosis was luetic aortitis which was confirmed by post-mortem examination.

CASE 28.—A seventy-three-year-old sailor entered the hospital complaining of dyspnea and scaling eruption of the lower legs. There was a history of lues at the age of twenty-three. Examination showed marked evidence of aortic insufficiency. Autopsy showed luetic aortitis.

CASE 30.—A forty-nine-year-old white woman entered the hospital complaining of dyspnea. Past history was negative except for two miscarriages. Seventeen years previously there were ulcers of both eyes. No history of lues. One year ago she had fainting and dizzy spells with increasing dyspnea. Examination showed a moderately enlarged heart with no murmurs. There was evidence of old glandular tuberculosis of the neck and some involvement of the apices of the lungs. X-ray examination showed dilatation of the aorta. Wassermann was negative. Autopsy revealed chronic nephritis and luetic aortitis. In this case the x-ray findings and the other secondary features of the case should be sufficient to make one strongly suspect syphilis, even in the absence of a positive Wassermann reaction.

CASE 31.—A sixty-year-old white man entered the hospital with lobar pneumonia, from which he died in a few days. Examination of the heart was entirely negative. There was no history of lues and no previous symptoms indicating circulatory disease. Autopsy showed lobar pneumonia and luetic aortitis. In this case the syphilitic process was silent and there was no way of suspecting it during life.

CASE 35.—A thirty-year-old Italian entered the hospital complaining of weakness and dyspnea. There was a definite past history of rheumatic fever but not of syphilis. Wassermann test was negative. Examination showed an enlarged heart with signs of aortic insufficiency. During life he was considered as having rheumatic heart disease. At autopsy it was found that he had luetic aortitis. This presents an extremely difficult problem in differential diagnosis. The only way such errors might be avoided is if, on careful x-ray examination of the aorta, additional data could be obtained. In rheumatism the aorta remains essentially unchanged whereas in syphilis irregularities of contour or localized dilatations occur.

CASE 36.—A sixty-four-year-old woman entered the hospital complaining of shortness of breath and substernal pain. There had been two miscarriages and two children died in infancy. Examination showed irregular pupils and enlarged heart and increased supracardiac dulness. The left radial pulse was much greater than the right. Distinct pulsation could be seen in the second left interspace. Autopsy showed a syphilitic aneurysm of the ascending aorta with extension into the right ventricular wall. Here, despite the negative Wassermann, there were sufficient data to make a clinical diagnosis of syphilis of the aorta.

CASE 37.—A forty-six-year-old white man entered the hospital complaining of dyspnea, palpitation, and pain in the abdomen. There was no history of lues and nothing pointing to aortic disease on examination. Clinically, the diagnosis was

hypertension, hyperthyroidism, and acute cholecystitis. Pathological examination showed well-marked luetic aortitis. In this case, as in Case 31, it would be difficult to make a proper diagnosis in the absence of a positive Wassermann, as there was very little to make one suspect syphilis either in the history or on the examination.

SUMMARY

In this review of 40 cases of syphilitic aortitis as determined by post-mortem examination, the Wassermann reaction in the blood was negative in 12 instances. An attempt was made to analyze the means we have apart from the Wassermann test that would enable us either to diagnose the condition during life, or at least to avoid overlooking its possibility. When there is evidence of aortic insufficiency or definite evidence of aneurysm of the aorta, that should be sufficient to direct our attention at lues as a possible cause. The same may be said of a positive past history of syphilis and of evidence of syphilis of the central nervous system. There remained, however, 4 cases in which there was no history of syphilis and no evidence of either aneurysm or aortic insufficiency. Such cases might be diagnosed in life by more careful roentgenological study, by an occasional finding of a positive Wassermann only after a provocative test, combined with other clinical data that in general point to syphilis.

THE RELATION OF SYPHILIS TO HYPERTENSION (STATISTICAL STUDY)*

EMMET F. HORINE, M.D., AND MORRIS M. WEISS, M.D.
LOUISVILLE, KY.

PATIENTS are encountered who have syphilis and hypertension. What relationship, if any, exists between the two conditions? Do syphilitic patients exhibit hypertension to a greater degree than non-syphilitic patients? Is the incidence of syphilis greater among hypertensive individuals than among a group of controls? These are some of the questions that thus arise, and a cursory search of the literature reveals confusing statements concerning the etiological relationship.

The etiological importance of syphilis is stressed by Faught[1] who states that "syphilis is well recognized as a cause of hypertension." Stoll,[2] finding that of fifty cases of hypertension, 90 per cent gave either a positive Wassermann or luetin test or were known to have lues or to have children with hereditary syphilis, claims that hypertensive disease is the most common of the so-called "late" manifestations of hereditary syphilis. Brin and Giroux[3] are of the opinion that syphilis is one of the principal causes of arterial hypertension. Smith[4] asserts that syphilis is often associated with high blood pressure and that hypertension is also a frequent corroborative sign in such cardiovascular conditions as aneurysm and syphilitic aortitis. Mattei and Toinon[5] studied 210 hypertensives and found syphilis the only etiological factor in thirty cases.

Contrasted with the opinions just mentioned Pellissier[6] believes that there is no such clinical entity as syphilitic hypertension. Davison and Thoroughman[7] in a study of heart disease in the negro race state that in their series of cases with combined syphilis and hypertension syphilis *per se* had nothing to do with the causation of hypertension any more than another toxic or infectious condition might. Keith, Wagener and Kernohan,[8] finding a positive Wassermann only once in seventy-five cases of malignant hypertension, believe that syphilis is not etiologically important in this condition. Steinfield, Pfahler and Klauder[9] state that syphilis apparently plays no part in hyperpiesia, especially of the climacteric group. Fishberg[10] does not believe that syphilis is a causative factor in essential hypertension.

The incidence of syphilis in hypertension has been variously reported. For example McElroy[11] noted a positive Wassermann in only 5 of 100 cases of essential hypertension while Stone and VanZant[12] found that of 436 patients with hypertensive heart disease 28.3 per

*From the Medical Department, University of Louisville, School of Medicine.

cent had syphilis. McLester[13] found a positive Wassermann in 17.5 per cent of 124 patients with hypertension. R. F. Weiss[14] analyzed 56 cases of essential hypertension from an etiological point of view and found syphilis in 8.9 per cent of the cases. Palmer[15] found no instance of syphilis in 81 young male adults with a systolic blood pressure of 150 mm. Hg. or over. Vaquez[16] found syphilis to be present in 78 of 100 hypertensive individuals and Amblard[17] found syphilis in 78 per cent of his hypertensive patients. In a study of the cardiovascular findings in women with syphilis, Arnett[18] found that 8.3 per cent of the cases of tertiary syphilis had arterial hypertension as against 5.1 per cent of the control group.

Because of such conflicting statements as cited above, a study was undertaken of 666 cases of essential hypertension admitted to the wards of the Louisville City Hospital from 1925 to 1930. Two thousand control admissions were likewise studied. A positive Wassermann was considered evidence of a syphilitic infection; although we are well aware that syphilis may be present in an individual with a negative Wassermann. No attention was paid to the history alone of a primary sore or secondary eruption. Statements of our city hospital patients and especially negroes are notoriously unreliable in respect to such lesions. We included in our study only those cases which were sufficiently complete as to lend themselves to statistical analysis. No known cases of secondary hypertension were included. An especial attempt was made to exclude cases of chronic diffuse nephritis with coexisting hypertension from cases of essential hypertension with varying degrees of renal insufficiency. Where a differentiation could not be made in a given case, it was not included in the study. Although some nephritic hypertensive patients may have been included, they are probably too few in number seriously to affect the final conclusions.

A systolic pressure of 150 mm. Hg. or a diastolic pressure of 100 mm. Hg. constantly maintained was arbitrarily considered the lower limits for hypertension. No attempt was made to calculate the expected average blood pressure from the height, weight and age, since all the cases had a blood pressure well within the hypertensive level. An exception to this is a carefully selected group of 68 cases with normal or low blood pressure and cardiac enlargement but without any valvular lesion present or other factor that might produce the cardiac enlargement. We believe that such patients must of necessity fall in the hypertensive group even though the previous level of the blood pressure is unknown. Ophthalmoscopic signs of a preexisting hypertension frequently will be found. Roentgenologic examination may furnish suggestive proof of the presence of a previous hypertension because of the cardiac silhouette. In addition, impairment of renal function or even uremia may be present. Electrocardiographically marked left axis deviation and frequently the coronary types of elec-

trocardiograms are encountered here, such as are so often found in the known hypertensive individuals. While this type of electrocardiogram does not of itself evidence preexisting hypertension, its presence with an unexplained cardiac enlargement, eye-ground signs and findings of renal impairment, is suggestive evidence of the previous elevated state of the blood pressure. In hypertensive cases the development of a coronary occlusion results in a marked lowering of the blood pressure to normal or even subnormal levels. Furthermore, in twenty years of recorded blood-pressure observations we have had personal opportunity to watch certain patients who first merely presented hypertension, later gradually developed cardiac hypertrophy, still later presented electrocardiographic evidence of coronary changes and who, following an acute coronary occlusion or the onset of congestive heart failure, finally showed a marked lowering of the blood pressure. The arteriolarsclerotic or primary contracted kidney which always evidences a hypertension during the life of the individual will be found at autopsy in these cases. We have elsewhere reported (December 2, 1929) a selected group of such cases.[19]

Of the 666 patients studied, 526, or 79 per cent, had a negative Wassermann while 140, or 21 per cent, had a positive serum reaction. The group investigated included 369 negroes and 297 whites. Of the 369 negroes 112, or 30.4 per cent, had positive Wassermanns whereas only 9.4 per cent of the whites had serological evidence of the infection (Table I). The relatively high percentage of syphilis as found in the combined group is thus the result of the marked incidence of syphilis among the negro hypertensive patients.

Of a control group of 2000 Wassermann tests on patients aged thirty to ninety years in the various clinics and wards of the Louisville City Hospital, 25.5 per cent had a positive Wassermann. This compares fairly closely with the percentage incidence of syphilis in the hypertensive group. Of the negroes numbering 967 in the control group, 316 or 32.6 per cent had a positive Wassermann (Table II).

TABLE I

HYPERTENSIVES ANALYZED ACCORDING TO WASSERMANN REACTION AND RACE

WASS.	TOTAL	PER CENT	WHITE	PER CENT	NEGRO	PER CENT
−	526	79	269	90.5	257	69.6
+	140	21	28	9.5	112	30.4
	666		297		369	

TABLE II

CONTROL GROUP ANALYZED ACCORDING TO WASSERMANN REACTION AND RACE

WASS.	TOTAL	PER CENT	WHITE	PER CENT	NEGRO	PER CENT
−	1489	74.5	838	81.2	651	67.4
+	511	25.5	195	18.8	316	32.6
	2000		1033		967	

The difference in the incidence of syphilis in hypertensive individuals as noted by various observers thus largely depends upon the prevalence of syphilitic infection in the particular class of patients studied. McLester[13] found syphilis in 17.5 per cent of his hypertensives, because 16.5 per cent of his patients in general had a positive Wassermann. Palmer,[15] studying young college men, found no instance of syphilis in those with hypertension and his control group was similar, showing a syphilitic rate of only 0.8 per cent. Pellissier[6] encountered syphilis in 26 per cent of 60 cases of essential hypertension in contrast to an incidence of 20 to 22 per cent in the population as a whole.

Table III shows the distribution of cases of our hypertensive group according to sex. There was practically no difference in the incidence of syphilis in the sexes of both colors. Of the 392 males, 87 or 22.2 per cent, had a positive Wassermann as against 53 females, or 19.4 per cent. The white males had a syphilitic rate of 8.1 per cent in contrast with the negro male rate of 35.2 per cent and the female whites had a positive rate of 11.8 per cent against the female colored group with a rate of 24.4 per cent. In the control group the distribution of syphilis among the sexes of both the white and negro patients is practically the same as in the hypertensive group (Table IV).

TABLE III

HYPERTENSIVES ANALYZED ACCORDING TO WASSERMANN REACTION, RACE AND SEX

			Males			
WASS.	TOTAL	PER CENT	WHITE	PER CENT	NEGRO	PER CENT
−	305	77.8	172	91.9	133	64.8
+	87	22.2	15	8.1	72	35.2
	392		187		205	
			Females			
−	221	80.6	97	88.2	124	75.6
+	53	19.4	13	11.8	40	24.4
	274		110		164	

TABLE IV

CONTROL GROUP ANALYZED ACCORDING TO WASSERMANN REACTION, RACE AND SEX

			Males			
WASS.	TOTAL	PER CENT	WHITE	PER CENT	NEGRO	PER CENT
−	756	70.7	466	79.7	290	59.8
+	313	29.3	118	20.3	195	40.2
	1069		584		485	
			Females			
−	733	78.8	372	82.9	361	74.9
+	198	21.2	77	17.1	121	25.1
	931		449		482	

The distribution of the cases according to age is shown in Table V. The largest number of cases, 90 per cent, occurred in the fifth to the ninth decades inclusive, as occurs in hypertension in general. The

TABLE V

HYPERTENSIVE PATIENTS ANALYZED ACCORDING TO WASSERMANN REACTION, AGE, SEX AND RACE

AGE WASS.	20-29				30-39				40-49				50-59				60-69				70-79				80-89				90-99				TOTAL	
	M		F		M		F		M		F		M		F		M		F		M		F		M		F		M		F		M	F
	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N	W	N		
−	1	2	2	4	2	5	4	12	12	35	17	36	48	36	19	34	63	30	29	24	40	21	22	10	5	4	4	3	1	0	1	0	305	221
	3		6		7		16		47		53		84		53		93		53		61		32		9		7		1		1		77.8%	80.6%
+	0	1	1	1	1	8	1	3	2	16	4	18	4	32	3	9	5	11	4	6	2	4	0	3	1	0	0	0	0	0	0	0	87	53
	1		2		9		4		18		22		36		12		16		10		6		3		1		0		0		0		22.2%	19.4%
	12				36				140				185				172				102				17				2				392	274

highest incidence of patients with positive Wassermanns occurred in the fourth, fifth and sixth decades as might be expected.

A thorough study of combined syphilitic and hypertensive heart disease was not attempted. We are in accordance with Arnett, who believes that since the physical signs of syphilitic aortitis without aortic regurgitation are frequently found in patients with hypertension, it is impossible in most cases of syphilis with hypertension to determine clinically whether or not syphilitic aortitis is present. Fourteen cases with a positive Wassermann had frank aortic insufficiency without a high pulse pressure. Two of these patients had roentgenological signs of an aortic aneurysm, and the only case which came to autopsy showed a large aneurysm of the arch of the aorta with an extension of the process to the aortic valve producing an aortic insufficiency. We are unable clinically to determine in these cases of aortic insufficiency whether the hypertension or the syphilis or both were responsible for the valvular lesion. It is well known that syphilitic aortitis and hypertension may coexist. In a study of heart disease in the negro race, Davison and Thoroughman[7] found that of 65 patients with syphilitic heart disease, 16 had a coincident hypertension. Stone and Vanzant[12] in a survey of heart disease in a southern clinic state that at autopsy pathologists often demonstrated greatly enlarged hearts without valve defects so characteristic of hypertensive heart disease but with a coincident typical syphilitic aortitis. Smith[4] claims that hypertension is a frequent corroborative sign in such cardiovascular conditions as aneurysm and often in syphilitic aortitis. Fishberg[10] confirms Gallavardin's[20] observation that the combination of syphilitic aortitis and hypertension is uncommon.

The problem of the etiology of hypertension still remains an enigma. Janeway[21] has well said that the "range of possible etiological factors as found in the life history of patients was so great as to demand an extensive critical study to yield anything more than the usual textbook catalogue of all the diseases and vices of the human race." The French authorities have, in general, stressed the possibility that syphilis has an important bearing on hypertension. They probably felt that since syphilis attacks the heart and vascular system hypertension might be the expression of such invasion. Our present concept of essential hypertension as an arteriolar disease would seem to preclude any such possibility. Further, the microscopical findings in syphilitic involvement of the arteries are radically different from those in hypertension. Another reason why syphilis has been suspected as a cause for hypertension is the fact that in certain groups studied syphilis was the only condition found in the past history of the patient. However, we have shown that in carefully controlled groups syphilis has been an equally striking factor.

SUMMARY

A group of 666 patients with essential hypertension was studied to determine if syphilis were a possible etiological factor. A control group of 2000 nonhypertensive patients of similar ages and economic status was studied. The incidence of syphilis was practically the same in the hypertensive group as in the control group. Syphilis cannot have any etiological bearing on essential hypertension.

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CLINICAL HEART FINDINGS IN CHILDREN WITH CONGENITAL SYPHILIS

GIUSEPPE PREVITALI, M.D., GERTRUDE H. B. NICOLSON, M.D., AND D. MOON-ADAMS, M.D.
NEW YORK, N. Y.

REPORTS on the clinical heart findings in congenital syphilis are meager in comparison to the extended studies made on other phases of the disease. Pathological examinations, dating from Rosen's description in 1860 of gummata in the heart of a newborn infant, are fairly numerous and give a definite picture of changes in the myocardium and great vessels occasionally found at autopsies of congenital luetics. However, it is noteworthy that the great majority of such reports deal with fetuses or with infants of less than one year. The impetus given to the study of heart disease in acquired syphilis, when Heller in 1899 pointed out its relationship to aortitis, apparently did not extend to congenital syphilis. Moreover, there is divergence of opinion among those who have studied the subject as to frequency and manifestation of heart involvement.

Alfred Friedlander in a paper read before the thirty-third meeting of the American Pediatric Society in 1921, maintained that myocardial degeneration in children was frequently caused by syphilis and falsely attributed to other infections.

Stolkind[1] in 1920, after reviewing the literature, concluded that no proved case of aortitis in congenital syphilis had been reported and surmised that congenital syphilitics with heart involvement did not survive birth long enough to give clinical manifestations.

Warthin[2] reported a case of acute syphilitic myocarditis in a man of twenty-five years suffering from congenital syphilis. He also reported autopsies on two infants who showed spirochetes in the heart muscle with absence of any other luetic lesions, and suggested that this may be a more frequent cause of sudden death than is commonly recognized.

Matusoff and White[3] published a pathological study of 35 cases of congenital syphilis autopsied at the Massachusetts General Hospital and the Infants and Child Hospital in Boston, and a clinical study of 25 cases under treatment. Fourteen, or 40 per cent, of the first group showed luetic changes in the heart or blood vessels. In the second group studied for clinical signs they found no cardiac involvement attributable to lues.

In view of such conflicting reports, we thought it of interest to examine the heart in fifty cases of congenital syphilis, under active treat-

ment at Bellevue. Our plan of procedure was first to verify the diagnosis of congenital syphilis by physical signs and by a family history and blood tests on the parents and siblings. The past history of each case was thoroughly investigated to eliminate the possible complication of rheumatic infection, and no child in this group had had endocarditis, acute rheumatic fever, joint pains, frequent sore throats or chorea. Only four gave histories of occasional sore throats. In one an effusion without fever or redness was present in both knee joints which cleared up under antiluetic treatment and was diagnosed luetic arthritis.

Complete physical examination was made recording the general constitution and habitus of the child. Teleroentgenograms and electrocardiograms were taken on each patient. Record was made of treatment received prior to examination, the age at which treatment was started, the blood Wassermann report on admission and also at the time of examination. Finally the cases were grouped by their age and sex.

Our study included 28 girls and 22 boys; the youngest was four weeks of age and the oldest fourteen years. Forty-six of the 50 were under eleven years, 14 under two years and 9 under one year. In every case the blood Wassermann was 4 plus on admission. At the time of examination 32 cases had 4 plus Wassermann reports, 3 had 1 plus, 1 had 2 plus and 14 had negative Wassermanns.

The latter group comprised children who had been under treatment for varying periods extending from three months to twelve years. Seven children were examined before receiving treatment.

The group showed no symptoms of tachycardia or dyspnea on exertion, or other signs suggesting a cardiac syndrome. On physical examination of the heart no abnormal pulsation, precordial bulging, marked venous tracing or cyanosis was noted. No instance of clubbing of fingers or toes was seen. The point of maximum cardiac impulse was found in each case to be within normal limits, and the percussed borders showed no enlargement. On auscultation no murmurs of organic type were heard. In eight cases systolic murmurs were heard at the base or apex which, because of their location, their lack of transmission and variable intensity were classified as functional. To record blood pressure a sphygmomanometer with child cuff was used and readings were taken from the arm, or in small infants from the leg. Eleven readings have been omitted from this study, judged inaccurate, in one instance because the patient had an evident glandular dyscrasia as a basis for his hypotension, and in the others because a uniform reading seemed impossible on account of the constant crying of these infants. In the remaining 39 cases the average pressure was

93 mm. systolic with a diastolic of 51 mm., giving an average pulse pressure of 42 mm. This is somewhat higher than that found in normal children. Our highest systolic blood pressure was 125 in a boy of nine years and the lowest 82 in a girl of two years. The diastolic pressure was audible to zero in three children, but as a change in the intensity of the pulsation was heard at a some higher level, this degree was taken as the diastolic reading.

The roentgenograms were taken at a distance of six feet except in nine infants on whom flat plates were made. The sthenic type of heart predominated, being present in 28 cases. Hypersthenic hearts were seen in 6 cases and hyposthenic in one. Among the 9 infants on whom flat plates were taken no apparent enlargement was seen. The 35 teleroentgenograms showed no increase in the ratio between the transverse diameter of the heart and that of the pulmonic field except in two instances where the hearts were of the hypersthenic type.

In twelve cases the right auricular curve and in one both auriculars were accentuated. In one instance the left auricular and the left ventricular curve, and in another the ventricular alone was accentuated. Two children with negative clinical findings showed an accentuation of the curve of the pulmonic artery. No case showed widening of the aortic arch.

Electrocardiograms were obtained on all of the 50 children. Their rhythm was of the regular sinus type in all instances. In one case, a crying infant, this was interrupted by occasional premature auricular contractions. Sinus arrhythmia was frequently present, simple tachycardia was noted nine times, and bradycardia once. Low voltage was noted in 14 records. Conduction between auricles and ventricles was in no case delayed; there was no defect found in the bundle or its branches. Axis deviation was equally distributed, being present five times to the right and five to the left. The individual deflections did not differ from the normal. P_3 was not found inverted and T_1 and T_2 were always upright. The R-wave in Lead I was commonly of poor amplitude.

SUMMARY OF FINDINGS IN FIFTY CASES OF CONGENITAL SYPHILIS

1. Physical examination of the heart was negative.

2. Rheumatic lesions were not present.

3. Average blood pressure was 93/51, giving a pulse pressure of 42, the normal being from 27 to 30.

4. Thirty-five teleroentgenograms showed normal ratio between transverse cardiac diameter and pulmonic fields. The aortic arch was in no case widened.

5. Electrocardiograms showed normal rhythm with no delay in conduction, no abnormalities of deflection, but frequent low voltage.

6. The findings in children who had received no treatment were the same as in those whose Wassermanns had been rendered negative by treatment.

7. Children of varying age groups showed no differentiation in their physical signs.

CONCLUSION

In contrast to the findings in acquired syphilis, we were not able to detect, by available methods of physical examination, any cardiovascular lesion in the fifty cases of congenital syphilis examined.

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HEART DISEASE IN CHILDREN DUE TO CONGENITAL SYPHILIS*

THURMAN B. GIVAN, M.D.
BROOKLYN, N. Y.

MY CONTRIBUTION to this symposium consists in the analysis of more than four hundred cases of congenital syphilis. These were selected from cases with outstanding symptoms of the disease, such as young infants with florid skin and visceral lesions, the older child with interstitial keratitis, joint signs, or central nervous symptoms. The total number of cases of this disease observed during the past ten years exceed two thousand. In collecting this data, autopsy records, x-ray reports, electrocardiographic reports, laboratory findings, etc., were used from the Long Island College and Brooklyn Eye and Ear Hospitals. Most of the cases have been observed for several years, and a majority have had a cardiac examination during the past two years. Until two years ago very little attention was directed to the heart in these cases; however, clinical examinations were done on practically all cases, as well as on those in this series. When the *Spirochaetae pallidae* invade the blood stream of the unborn infant, obviously, a septicemia begins, and, depending upon several factors, for example, the virulence and the selectivity of the invader, vital organs and tissues of the body are injured. This injury seems to vary in degree; hence anything from a macerated fetus to a perfectly well-developed, living infant may be delivered. Autopsy records in the former show the *Spirochetae pallidae* in the various tissues of the body, notably the liver, the spleen, the lungs, the osteochondral portions of the long bones, and many times in the heart, particularly the myocardium. These infants, if not born dead, usually die during the first three or four months after birth, with or without treatment.

In no case has the autopsy protocol shown sufficient changes in the heart to account for death, although interstitial myocarditis and vacuolization of the muscle fibers have been demonstrated. Usually a terminal pneumonia and now and then a syphilitic meningitis account for death. Except to the pediatrist and the syphilologist these cases are only of academic interest. The question you are interested in is, what happens to the heart and aorta of the child with congenital syphilis as he grows up? Undoubtedly some of these infants with spirochetal invasion of the heart and other visceral organs, if treated early, survive and actually do grow up.

*From the Department of Pediatrics, Long Island College Hospital, Brooklyn, and the Congenital Syphilis Clinic of the Brooklyn Eye and Ear Hospital, Brooklyn.

Table I shows 404 cases of congenital syphilis divided into age groups. One hundred and seventeen had a physical examination with especial reference to their hearts before receiving any antisyphilitic treatment. Many had x-ray, fluoroscopic, electrocardiographic, blood pressure and clinical examinations. In no case was anything referable to cardiac damage found. Likewise 287 patients who had received antisyphilitic treatment had similar examinations; in none of these did the heart show any abnormalities. The fact that the pulmonic second in children presents normally a louder sound than the aortic second was an aid in reaching the above conclusion. Any case showing A_2 equal to or louder than P_2 was selected for a more careful survey. The older the age group, naturally, the more were there of these cases.

TABLE I

NO SIGNS OF HEART DISEASE

AGE	UNTREATED CASES	TREATED CASES	CASES WITH INTERSTITIAL KERATITIS
Under one year	8	5	0
Between 1 and 2 years	4	3	0
Between 2 and 5 years	17	15	13
Between 5 and 10 years	44	78	51
Between 10 and 16 years	36	133	96
Between 16 and 30 years	5	48	45
Over 30 years	3	5	7
Total	117	287	212

Those showing interstitial keratitis are included in the tabulation for the reason that these cases occur usually only as a lighting-up process in congenital syphilis tarda. During this period of activation one might expect cardiac changes, but in our experience such is not the case.

Taking for granted that syphilitic heart changes take place on an average of eighteen to twenty years after the primary infection in acquired syphilis, a special effort was made to follow up those cases of congenital syphilis more than sixteen years of age. Sixty-one of such showed no cardiac abnormalities.

It might be said of the 287 treated cases that some of these might have developed heart changes had they not been treated. This obviously cannot be answered. Many of them, however, had been examined previously, a large number during infancy, with no notation of cardiac disease.

Syphilologists who have had large experiences in treating organic heart conditions due to syphilis tell us to beware when using the arsenicals in such cases. In our experience we have never encountered a single instance of having to suspend this drug on account of cardiac symptoms. Only three deaths[1] in patients over six months of age have

occurred in more than two thousand cases that have been treated in my clinics. Autopsy on two of these showed no cardiac abnormality, and the other child showed no evidence of a cardiac death.

Eight cases of our series showed organic heart disease. Three of these, four months, eleven months, and twenty-six months of age, respectively, had congenital heart lesions; two probably pulmonic stenosis, and the youngest probably a patent ductus arteriosis. All three had 4+ Wassermanns and came from families with definite syphilis. Whether congenital syphilis played a part in these cases is not known. Only autopsies would have revealed definite evidence. The other five

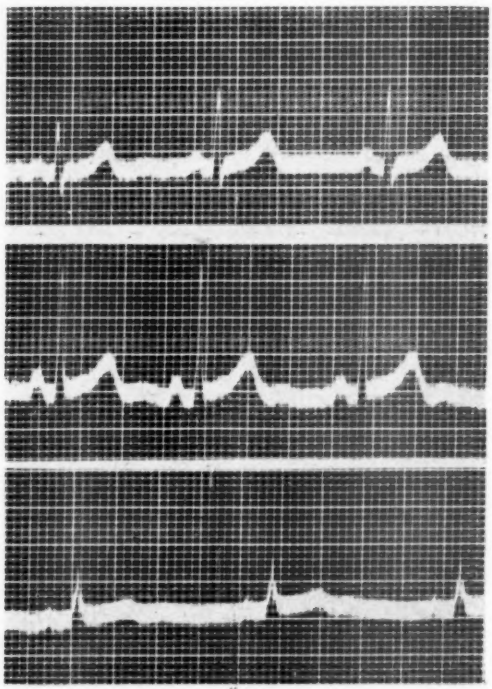

Fig. 1.

cases showed histories, symptoms, physical signs and other data which led to a diagnosis of mitral disease of a rheumatic nature. Three other congenital syphilitic children showed chorea but without positive heart findings. A nine-year-old boy with a 4+ Wassermann was diagnosed from eye findings and a blood pressure of 145/90 mm. as having juvenile arteriosclerosis. His heart was normal so far as physical signs, electrocardiogram and x-ray were concerned.

The only case with heart findings that might be classified as being due to congenital syphilis is that of an eight-year-old girl with active interstitial keratitis, with a 4+ Wassermann, and with a positive family history of syphilis. Her aortic second sound was very loud and

almost ringing in character at times. There was no murmur at the base but a definite systolic soft blow at the apex transmitted to the left anterior axillary line. X-ray showed no abnormality. The heart was not enlarged and caused her no embarrassment. The electrocardiogram (Fig. 1) shows no abnormality with the exception that the S-T interval comes off 1 mm. below the base line in Lead I and 1 mm. above the base line in Leads II and III.

COMMENT

Four hundred and seventeen cases of congenital syphilis ranging in age from three months to forty-two years were studied with reference to heart disease being caused by the *Spirocheta pallida*. Up to the present moment not one of the cases has shown signs or other collected data that would lead one to make a definite diagnosis of syphilitic heart disease.

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DISCUSSION

Dr. H. E. B. Pardee, New York, N. Y.—Although Dr. McCulloch* has not been able to present his paper today, I believe from my correspondence with him that he is able to report very much the same sort of findings as have been recorded by Dr. Givan and Dr. Previtali. He was not able to find an appreciable amount of cardiovascular disease in these children. In connection with this finding it must be remembered that these children represent a very different type of case from those which have been discussed here today, who are suffering from cardiovascular disease, and who apply for treatment. These children represent so many exposures to the infecting agent of syphilis, and it should not be expected that the incidence of cardiovascular involvement would be great. We do not know what percentage of adults infected with syphilis go on to develop lesions of the cardiovascular system. It is likely that only a small percentage does so, and so we should not be surprised if the amount of cardiovascular syphilis in children with hereditary infections is not great.

*McCulloch, Hugh: Congenital Syphilis as a Cause of Heart Disease, see p. 136.

CONGENITAL SYPHILIS AS A CAUSE OF HEART DISEASE*

HUGH MCCULLOCH, M.D.†
SAINT LOUIS, MO.

INTRODUCTION

IT IS known that syphilitic infection is followed in many instances by localization of the disease in the heart or large blood vessels of the human body. Even when the infection is recognized early and treated carefully, cardiac and vascular complications may occur five, ten or more years later in life; and in unrecognized or untreated cases, the frequency of these late lesions in the heart and blood vessels is known to increase. Just how probable the occurrence of syphilitic heart disease in a given individual will be, cannot be stated accurately. Conservative estimates would place the frequency at about 25 per cent in untreated cases and lower in well-treated cases. Since syphilitic infection of infants before birth from a syphilitic mother is a common disease and since the course of this type of syphilis is comparable in many ways to an infection acquired later in life, one would suspect that those children would frequently show signs of heart disease. A group of children with congenital syphilis has been studied to note whether or not this same tendency existed for the heart to become the seat of the disease following fetal infection. Many children are born while in the stage of infection which is comparable to the secondary stage of acquired syphilis, and a smaller number live to reach the stage comparable to tertiary syphilis of the adult.

LITERATURE

Interest in this study was increased by many reports in the literature on the probability of such an infection in fetal life resulting in heart disease both during childhood and also later in life. Warthin[1] has directed attention to the probability of sudden death from a latent syphilitic myocarditis, a type of lesion that is known to occur in children. Other acute infections in childhood, such as diphtheria, scarlet fever, and typhoid fever, are known to be followed by a myocarditis which may be the cause of sudden death in later life. Warthin also has well described the lesions to be found in the heart. He reported[2] twelve cases of congenital syphilis, nine occurring in infancy and early childhood, three in children after puberty all of whom showed the presence of the disease in heart muscle tissue. He was able to demonstrate the spirochete in the tissue even in the absence of histo-

*Read by title.

†From the Department of Pediatrics, Washington University School of Medicine and the St. Louis Children's Hospital.

logical lesions or spirochetes elsewhere in the body. In his description[3] of the histological findings, he states that in every case he has found fatty degeneration of the heart muscle to be present either as a diffuse fatty change or as a focal process. He says that as far as the organism of syphilis is concerned, it may cause a focal or a more diffuse degeneration of the myocardium before any interstitial changes occur, a purely parenchymatous change in the heart muscle. This lesion may heal without an interstitial reaction or focal fibroid areas as well as focal calcification of the degenerated muscle fibers can follow the primary lesions of the myocardium. The latter process would constitute changes responsible for heart disease in later life. Three cases described in older children were examples of this. One case had a history of old cardiac disease without a rheumatic infection, the other two showed decided underdevelopment.

There are numerous reports of cases of heart disease occurring among congenital syphilitic children. Fournier[4] has directed attention to the fact that various heart malformations may occur in subjects of hereditary syphilis. Case reports by Anderson[5] and Neugebauer[6] have been made. A collective review of cases with a report of an additional case has been made by Stobie.[7] deStefano[8] reports 32 cases of children with congenital malformations of the heart who were admitted to the Children's Clinic at Naples in the previous six years. Seventy-two per cent presented unmistakable signs of inherited syphilis and it was probable in all the others, except 5. His report does not include an examination of the heart muscle tissues for the presence of spirochetes or the histological changes of syphilis described by Warthin. The blood Wassermann test was positive in 27 of the 32 cases. Many of the heart malformations described were similar to those which may be found among children who do not have congenital syphilis; for example, patent foramen ovale, ductus arteriosus, or interventricular septum. Hahn[9] discusses the relationship between congenital syphilis and heart disease in early life of 130 cases of congenital syphilis and syphilitic fetal injuries. A large number, 80 to 90 per cent, showed a pure mitral stenosis. He regards the stenosis as evidence of retarded growth of heart muscle tissue following the syphiltic infection. Subjective symptoms were very slight and decompensation was never observed unless the stability of the anatomical condition was disturbed by bacterial infection of the valve.

Fordyce[10] describes 9 children with rheumatic heart disease who were also congenital syphilitics and in whom the striking feature was the absence of clinical signs pointing to the presence of a syphilitic infection. He suggests that an important subgroup of rheumatic children can be defined in whom the rheumatic infection is superimposed upon congenital syphilitic infection and undetected and untreated syphilis.

MATERIAL

The group of cases which forms the basis for this report has been seen in the Washington University Dispensary, the out-patient department of the St. Louis Children's Hospital. As a part of the general pediatric clinic, the syphilitic children and cardiac children are cared for as special groups. On admission each child first is seen in the general clinic when he receives a physical examination and is then referred to the special group for further care. While attending the syphilitic or cardiac clinic, the child is examined frequently and among other things, the presence of signs of syphilis and the Wassermann reaction being noted on all cardiac children and the presence of signs of heart disease on all syphilitic children. It was recognized that there were very few children who belonged to both groups so that the high incidence of heart disease among syphilitic adults did not seem apparent in children. The experience in this clinic has been sufficiently large now to warrant a report of the situation at the present time.

During the ten-year period beginning with 1915 and ending with the end of 1924, there have been in all 40,470 children treated in the general pediatric clinic. Children admitted after this period have not been included in this study, since it was felt that recent admissions would not have been under observation long enough. During this same period a diagnosis of congenital syphilis has been made on 939 of these children, or 2.3 per cent. This group of children was divided into two groups: those under two years of age, 441, and those over two years of age, 498. A diagnosis of structural heart disease has been made on 458 children during this same period, or 1.1 per cent. This number does not include children with chorea or with potential heart disease.

Of the 939 syphilitic children, 124 are known to be dead. Of this number 53 died in the Children's Hospital and autopsies were performed on a total of 34; two of these were above the age of two years and 32 under two years of age. Among the 34 autopsies, a syphilitic lesion of the heart was found on the following three children:

CASE 1.—H. H., Children's Hospital No. 9738, aged three months. Clinical diagnosis of congenital syphilis with no signs of heart disease. At autopsy there was found a fibrosed atrophy of the right ventricle, hypertrophy and dilatation of the right auricle with a patent foramen ovale and ductus arteriosus. There was evidence of syphilis on microscopic section of the heart muscle.

CASE 2.—L. H., Children's Hospital No. A-1049, aged four weeks. Clinical diagnosis of congenital syphilis. At autopsy, the heart muscle was very pale and much enlarged and the foramen ovale was wide open. There was marked thickening of the epicardium with newly formed fibrous tissue in which were enmeshed great numbers of large mononuclear and lymphocytic cells. The muscle bundles of the heart were all widely separated with thick bands of the same character of tissue; the blood vessels large and small showed a marked fibrosis, thickening of the walls, and there was wide constriction of the lumen. Levaditi stains showed spirochetes.

CASE 3.—D. L. R., Barnes Hospital No. 8001, aged three months. Clinical diagnosis of hereditary syphilis, bronchopneumonia, septicemia, pneumococcus type IV. Post-mortem examination revealed a heart which weighed thirty-four grams, the musculature appeared normal. Microscopically, the bundles of heart muscle fiber are separated by bands of new forming connective tissue which in some instances are as broad as are the bundles of muscle fibers. There is also a mononuclear reaction throughout the section, the cells being to a great extent of the large mononuclear type. The cells are seen both between the bundles of muscle fibers and between the separated fibers. There is seen a similar connective tissue and cell reaction about the vessels in this section. In some instances, this being a rather marked change.

No one of the other 29 children under two years of age who were examined at autopsy showed evidence of heart disease. All of the 32 children showed extensive syphilitic disease in other organs and spirochetes could be demonstrated in the affected tissue. The clinical course and post-mortem examination of these children indicated that they were suffering from a generalized syphilitic infection and that death was probably due to the toxemia associated with the infection. No one of this group who died or of the total group of 441 children under two years of age showed signs of congestive failure of the heart or other cardiac symptoms during life or associated with death. This group of children under two years of life corresponds then to the group of adults with generalized syphilitic invasion of the whole body during the so-called "second stage" of the disease following a primary infection.

Children with syphilitic infection who live past two years of life show signs of the disease in a somewhat different manner. The common physical signs in this age group are keratitis, characteristic (Hutchinsonian) caries of teeth, deafness, and interstitial changes in such structures as the brain, liver, and bones. They rarely suffer from any toxemia, do not become acutely ill from the syphilitic infection, and usually die of some intercurrent infection. Of these children who lived to be over two years of age, there were 498 in this study and of this number two, T. S., Children's Hospital No. 16341, and S. S., Children's Hospital No. 651, died of heart disease and three others who have not died are known to have heart disease. The two children who have died also had a very definite history of rheumatic fever, chronic tonsillitis, and physical signs of the type of heart disease usually seen in rheumatic children. It could not be determined that the presence of the syphilitic infection contributed to the fatal outcome of the heart disease. They both had clinical signs of the syphilitic infection other than the heart disease. Three of this group, R. W., Dispensary No. A-75048, O. G., Dispensary No. 37873, and A. P., Children's Hospital No. 18185, were alive when last heard from, the latter at the age of seventeen years. These three children gave no history of rheumatic

fever though such a condition could have existed, for the heart disease was of the type usually seen in rheumatic children. The last child, A. P., when last seen showed almost no signs of heart disease, though during the hospital admission she had an acute pericarditis, enlargement of the heart with mild congestive failure, and mitral valvular disease. She had no signs of syphilis other than a positive blood Wassermann reaction. This group of five cardiac children in a total number of 498 with congenital syphilis is about the same frequency as would be found in any normal control group. This 1.0 per cent frequency coincides with the 1.6 per cent frequency of the total of 458 children with heart disease who were found among the total of 49,470 children admitted to the general clinic during the ten-year period included in this study. They correspond to the group described by Fordyce.[10]

SUMMARY

Of 40,470 children under fifteen years of age admitted to the outpatient department of the St. Louis Children's Hospital, during a ten-year period from 1915 to 1924 inclusive, 939, 2.3 per cent, were found to have congenital syphilitic infection and 458 were found to have recognizable heart disease. Of the 939 children with syphilis, 441 were under two years of age. It was possible to obtain autopsies on 32 children who died at this age period and 3 showed the presence of syphilitic heart disease. No one of the other 29 who died, or 409 who lived, had symptoms at any time referable to heart disease.

Four hundred and ninety-eight of the syphilitic children were over two years of age and of this number, 5, or 1.0 per cent, were known to have heart disease. Two of these 5 died but without post-mortem examination and 3 were living when last heard from. The signs of heart disease in these 5 children were similar to those seen in children with rheumatic heart disease but without syphilitic infection. This frequency of 1.0 per cent coincides with the frequency of 458 children (1.1 per cent) with heart disease among the total of 40,470 children admitted to the general clinic, or in other statistical surveys of the incidence of heart disease among normal or control children.

No one of the children up to the age of fifteen years of life has died suddenly or showed signs of heart disease similar to syphilitic heart disease seen in adult or later life. The observations made on routine examination of this group of children were not done with the idea of proving the existence or nonexistence of a causal relationship between congenital syphilis and heart disease. The number included seems large enough to represent a satisfactory experience in a general Children's Clinic.

CONCLUSIONS

There is no evidence in this study that congenital syphilis contributes to the incidence of heart disease in children up to the age of fifteen years. That heart disease and sudden death may follow this type of infection later in life is not made clear by this study, but it may be supposed that instances of this sequel would be about equal to those that follow other acute infections of childhood.

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THE USE OF INTRAVENOUS ARSENICALS IN THE TREATMENT OF CARDIOVASCULAR SYPHILIS*

LAURENCE E. HINES, M.D., AND JAMES G. CARR, M.D.
CHICAGO, ILL.

THE infrequency in recent years of reported clinical studies on the treatment of cardiovascular syphilis might lead to the impression that all questions pertaining to the management of the disease are answered. On the contrary there are differences of opinion, not only regarding the method of administering antisyphilitic drugs, but also as to the advisability of giving these drugs to syphilitic patients with heart disease. Thus we are sometimes cautioned that intravenous arsenicals may seriously damage the myocardium when a preexisting myocardial insufficiency exists; that large aneurysms may increase in size or rupture under the influence of arsenicals; that coronary sclerosis or nephritis is a contraindication to the drug. This clinical report seems justified because we believe it contains some hitherto unrecorded observations on the use of intravenous arsenicals in cardiovascular syphilis. The studies, covering a period of eight years, have been made on patients who have been observed personally in the heart clinic of Northwestern University. During the eight-year period, one hundred and eight patients have been classified as having cardiovascular syphilis; eighty-eight are included in this study; twenty have been discarded either because the diagnosis was uncertain or because they did not receive neoarsphenamine during the time they were observed.

The criteria for the diagnoses made here are: definite aneurysm of the aorta with or without positive blood Wassermann; aortic regurgitation in patients with positive blood Wassermann; persistent systolic murmur over the aortic area in the presence of positive Wassermann; symptomatic evidence of heart failure or angina pectoris, or paroxysmal dyspnea in patients who have positive blood Wassermann.

Arbitrarily all cases have been classed as belonging to one of four groups, viz., simple aortitis, aortitis with aneurysm, aortitis with aortic regurgitation, and syphilis involving chiefly myocardium or coronary arteries. Of course, there are many cases with combined lesions, such as a combination of aneurysm and aortic regurgitation. In these instances the patient was grouped by the lesion which we considered had produced the outstanding symptoms. For example patients who presented peripheral vascular changes of aortic regurgitation, huge heart, signs of heart failure and incidentally, x-ray evidence of an-

*From the Cardiac Clinic of Northwestern University.

eurysm, were classed as aortitis with aortic regurgitation. The myocardial and coronary group includes only those patients who had no aortic regurgitation or aneurysm and yet presented signs of heart failure or symptoms of angina pectoris.

Technic.—All patients received a preliminary course of potassium iodide and mercury or bismuth. If the patient had heart failure, digitalis and rest were prescribed. After using iodide and mercury for from four to six weeks, neoarsphenamine was given intravenously at weekly intervals for eight to twelve weeks. The initial dose was 0.15 gm., the second dose 0.3 gm., subsequent doses were not higher than 0.45 gm. Following this series more bismuth or mercury for six to eight weeks and then alternate series of mercury and neoarsphenamine for a year. This plan was not consummated in all patients. If their symptoms or signs became aggravated, the treatment was discontinued. Others neglected to complete the full course. The average length of treatment was ten months, the shortest period two months, the longest, six years. The beneficial effects of the treatment were chiefly symptomatic, not anatomical. An aneurysm or deformed aortic valve will probably never change under any form of treatment. An arrest of the active inflammatory focus is the hope of the treatment.

TABLE I

	NO. OF CASES	FUNCTIONAL (AM. HT. ASSN.)			IMPROVED	STATIONARY	WORSE
		1	2a	2b			
Simple aortitis	46	2	38	6	33	11	2
Aortitis with aneurysm	17	1	14	2	7	5	5
Aortitis with aortic regurgitation	22		11	11	9	10	3
Myocardial or coronary	3		2	1	1	2	

Table I summarizes the effect of neoarsphenamine on the symptoms of eighty-eight patients. The effect cannot be considered a pure one in all cases because digitalis and other drugs were mixed if they were indicated. As shown in the table, sixty-six patients were functionally graded 2 a (American Heart Association), nineteen as Grade 2 b, and three as Grade 1. Many of the patients in Grade 2 b were hospitalized as a preliminary measure; and although extra caution was observed with these patients, we did not consider the advanced state of the disease as a contraindication to the use of neoarsphenamine. No patients in this series were classed as Class 3.

Forty-six patients were classed as simply aortitis; thirty-three, or 72 per cent, showed temporary clinical improvement. Seventeen were classed as aortitis with aneurysm; seven, or 41 per cent, were temporarily improved. Twenty-two were classed as aortitis with aortic re-

gurgitation; nine, or 40 per cent, were temporarily improved. Three were classed as myocardial or coronary syphilis; only one showed improvement. Fifty of the entire group of eighty-eight patients were clinically improved; twenty-eight, or 31 per cent, were not influenced by the drug. The patients studied were judged improved, stationary or worse by comparing the symptoms and findings before and after neoarsphenamine treatment. The effect on the prominent symptoms is analyzed in Table II. It shows: Pain a complaint by forty-four patients, relieved in twenty-five, unchanged in fourteen, and aggravated in five; dyspnea a complaint in forty-eight, improved in twenty-eight, unchanged in thirteen, aggravated in seven; palpitation a complaint by twenty-four, relieved in thirteen, unchanged in seven and aggravated in four; murmurs present in seventy-five patients showed improvement in four, no change in sixty-three, aggravation in eight; urinary findings (albuminuria and casts) present in sixteen patients improved in eight, unchanged in six and aggravated in two. The Wassermann reaction, positive at the start of treatment in eighty-five patients, was rendered negative in twenty-three patients, became less strongly positive in three and was uninfluenced by the treatment in sixty-two.

TABLE II

	PAIN	DYSPNEA	PALPITATION	MURMURS	URINARY FINDINGS	EDEMA	COUGH
Total cases with symptom	44	48	24	75	16	17	15
Relieved or improved	25	28	13	4	8	9	6
No effect	14	13	7	63	6	5	5
Aggravated	5	7	4	8	2	3	4

As mentioned previously, the symptomatic improvement was temporary. The average period of relief was about fourteen months, varying from two months to five years.

The recorded improvement in murmurs of four patients was a lessened intensity of basal murmurs in two and a disappearance of aortic diastolic murmurs in two. The latter interesting observation, occurring in two decompensated patients after compensation had been established, can best be explained by attributing the murmur to a relaxed aortic ring. With compensation established, the tone of the aortic ring is improved, and the regurgitant murmur disappears.

The improvement in urinary findings coincided with the improvement in edema and probably indicated that the albuminuria was due to renal passive congestion.

The table records ten patients who became symptomatically worse. In three there is evidence of actual anatomical damage by neoarsphen-

amine. The kidneys of one patient, whose case is cited later, were probably damaged. Another case, also described in detail, showed marked increase in signs of aortic insufficiency. Another patient developed acute red atrophy of the liver and died. No cases of sudden death or aneurysmal rupture were observed.

CASES TO ILLUSTRATE HARMFUL EFFECTS

CASE 1.—L. O., colored man, forty-one years old, referred to cardiac clinic Nov. 28, 1924, from an industrial plant, because the company physician had discovered a murmur. In December, 1922, an examination by the same physician had revealed no heart abnormalities. He had no complaint except weight loss of ten pounds in three months. Examination revealed the heart enlarged to the left (14.5 cm.) in the sixth interspace, a distant diastolic murmur over aortic area, positive Duroziez's sign, systolic blood pressure 118 mm., diastolic 70, Wassermann three plus and x-ray evidence of aneurysm of aorta. Mercurial rubs and iodides were administered from December 1 to December 28. Then he received three doses of neoarsphenamine (0.3 gm.) at weekly intervals. After the third dose, the diastolic murmur became definitely more harsh, the blood pressure changed to 120/60 mm., and slight substernal distress was noted. Neoarsphenamine was then discontinued because it was felt that the organic changes were progressing in spite of treatment and perhaps were aggravated by the treatment.

CASE 2.—E. L., colored, forty-five years old, who previously had generalized anasarca, presumably the result of heart failure, was given 0.3 gm. neoarsphenamine on November 28, 1929, after a preliminary course of mercury and iodides. Prior to the injection there were no urinary findings, and blood pressure was 110/60 mm. Two days later edema of the ankles and eyelids developed, and albuminuria and urinary casts were found. Edema soon became generalized and persistent. The blood pressure rose to 160/100. The nephritis persisted for three months.

CASES TO ILLUSTRATE TEMPORARY CLINICAL IMPROVEMENT

CASE 3.—A. T., white, laundryman, aged fifty years, when first observed August 30, 1926, complained of severe boring substernal pain, dyspnea and palpitation. Examination revealed an enormous aneurysm of the arch and of the descending aorta (x-ray). The heart was not enlarged; the tones were clear except for a soft systolic murmur at the base. Iodide, mercury and analgesic drugs were used for ten weeks, and there was no relief from the severe pain. Striking pain relief was noted the day after one dose of neoarsphenamine was given. He remained in relative comfort for nine months, receiving during this period twenty-four injections of neoarsphenamine (0.3 gm.). During this period he received also potassium iodide. The final outcome of this case is unknown because the patient left the city.

CASE 4.—J. D., a white male, sixty years old, entered the clinic October 12, 1928, complaining of dyspnea, cough, and generalized edema. Asthmatic attacks had been present for a year, dyspnea and edema for three months. Gonorrhea and syphilis were acquired sixteen years before. Examination revealed a man acutely ill, with labored breathing, blood pressure 180/110 mm., generalized soft edema, huge heart with marked increase of mediastinal dullness, systolic and diastolic murmurs over the aortic valve, pulsating palpable aneurysm of the right carotid artery and four plus blood Wassermann. He was sent to Wesley Memorial Hospital where he remained until January 30, 1929. On discharge he had no dyspnea, pain, or edema. While in the hospital, the treatment consisted of digitalization, a course of iodide and mercury followed by weekly injections of neoarsphenamine, which were

continued until July 15, 1929. About three months after the treatment was started, the diastolic murmur disappeared. On July 25 the Wassermann was negative. In September, 1929, dyspnea, cough and pain developed but were relieved when he returned to the hospital. In January, 1930, after another series of neoarsphenamine treatment the Wassermann had become four plus. Symptoms of decompensation recurred February 7, 1930, and became worse until death on March 5, 1930. This case illustrates the symptomatic improvement which occurred in a man who received neoarsphenamine while suffering from cardiac decompensation. Although the improvement was temporary, we believe that the use of the drug in this case, as in others, caused some prolongation of life.

SUMMARY

A clinical study on the effect of neoarsphenamine on the symptoms of patients with cardiovascular syphilis is presented. Symptomatic improvement is believed to be a neoarsphenamine effect in 57 per cent of the cases. Twelve per cent showed aggravation of symptoms; probable anatomical damage was produced in three patients. No cases of sudden death or aneurysmal rupture were noted. A higher percentage of improvement is noted in patients who have syphilitic aortitis without definite aneurysm or aortic regurgitation. If the drug is cautiously administered in small doses, patients functionally classed 2 b (American Heart Association) may be benefited by the drug.

Improvement in the serological reactions of the blood does not always parallel the symptomatic improvement. Although the lives of patients with cardiovascular syphilis are perhaps prolonged by neoarsphenamine treatment, there is no evidence in any case studied which shows that the disease was permanently arrested.

DISCUSSION

Dr. Alexander Lambert, New York, N. Y.—When salvarsan first came out, a full dose used to be given to the syphilitic individual with cardiac disease or with aneurysm. These patients did well for about six weeks. Then we saw cases where the patient suddenly dropped dead without warning. The effect had been that of degeneration of the wall of the aneurysm. After that we never gave a dose of more than 0.1 gram, and always accompanied with mercury and iodide. Salvarsan was given once a week, and in that way there were not so many accidents. The patients were usually distinctly improved, but there were other cases that did not improve. It must be emphasized that the amount should never exceed a small dose given at five or six-day intervals. The drug does stop pain more quickly than any other thing in syphilitic aneurysm.

Dr. F. N. Wilson, Ann Arbor, Mich.— I have seen two or three patients with luetic heart disease in whom arsphenamine therapy was promptly followed by striking changes in the electrocardiogram. These changes were either permanent or persisted over a long period.

Dr. Norris, Springfield, Ill.—In the patients with some degree of heart failure, and treated with arsphenamine, what was the duration of life subsequent to treatment?

Dr. A. G. Sullivan, Hot Springs National Park, Ark.—Preliminary treatment should be stressed, as it is a very important factor. In the U. S. Public Health Service Clinic at Hot Springs a routine treatment is used consisting of three intra-

muscular injections of mercury and two injections of salvarsan weekly. We find that as a result of routine treatment (without careful cardiac examination) we had several deaths attributable to salvarsan. Autopsy showed scar tissue formation around the coronary openings. As a result we gave to our cardiac patients considerable preparatory treatment (at least a month) with mercury and iodides before starting salvarsan in small weekly doses, and since then we have had no deaths attributable to the treatment. In judging the length of preparatory treatment, cases already showing some interference with intraventricular conduction by slurring, notching or widening of the QRS complex should have more preliminary treatment. Unfortunately, mercury and iodides alone will not stop the progress of aortitis. Something more has to be done. In those cases which we feel are not suitable risks for salvarsan we are using bismuth. Its exact value in the treatment of cardiovascular syphilis is still undetermined.

Dr. W. H. Robey, Boston, Mass.—I thoroughly appreciate what Dr. Sullivan said. Whether there is much cardiovascular disease or not, if a middle-aged patient has syphilis, the physician should proceed with caution.

Dr. Hines (closing).—Electrocardiograms were made at the time of first admission to the clinic. No analysis was made of this work. In patients who were edematous the period of improvement was short. One man remained well a year. That was the longest period of relief noted in this group. Mercury and iodide were used before arsphenamine was started.

THE TREATMENT OF CARDIOVASCULAR SYPHILIS

A Study of the Duration of Life in 141 Treated and Untreated Patients With Aortic Regurgitation and Aortic Aneurysm*†

Joseph Earle Moore, M.D., and James H. Danglade, M.D.
Baltimore, Md.

THE treatment of cardiovascular syphilis is a controversial subject on which there are as yet wide differences of opinion, ranging from deepest pessimism to unbounded optimism. One school of thought holds that treatment should be limited to such medical measures as rest, restriction of activities, diet, and digitalis, and that if antisyphilitic treatment is given at all, it should be confined to the iodides and mercury by mouth or by inunction. The opposite viewpoint is held by others who, while conceding the value of conservative treatment, nevertheless feel that the arsenicals and bismuth may be added to the treatment armamentarium without risk and with marked benefit. The literature upholding one or other of these points of view is voluminous, but is based almost entirely on impression or opinion, much of which is unconvincing to the skeptic. We are unable to find adequate reports appearing since the introduction of modern methods of syphilotherapy, which deal with the question of the possible prolongation of life in a series of treated as compared with a series of untreated patients with cardiovascular syphilis. We shall attempt to supply this deficiency, limiting the discussion of our material to this major point, and, owing to the limitations of time and space, avoiding a discussion of the literature, which will be considered in some detail in a subsequent communication.

THE MATERIAL OF THIS STUDY

The primary interest of the syphilologist, so far as cardiovascular syphilis is concerned, lies in the question of early diagnosis and, by means of adequate treatment, the prophylaxis of its later manifestations. For this reason he is particularly prone to make the diagnosis of syphilitic aortitis on the basis of symptoms (substernal pain or oppression, paroxysmal dyspnea), with physical findings (increased retrosternal dullness, accentuated ringing aortic second sound in the absence of hypertension, etc.), and teleroentgenographic evidence of a widened inelastic aorta, in the absence of any valvular insufficiency. He is supported in this attitude by the great frequency of aortic lesions

*From the Syphilis Division of the Medical Clinic, the Johns Hopkins Hospital.
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at necropsy in syphilitic patients, so that the presumptive diagnosis is more often right than wrong. However, it is also true that aortitis diagnosed during life is often absent at necropsy; and this experience is so frequent that many internists are unwilling to accept the clinical diagnosis of syphilitic aortitis unless the patient has a definite aortic regurgitation or an aneurysm. The clinical differentiation of syphilitic myocarditis as an isolated lesion from other diagnostic possibilities is also extremely difficult. In order to avoid introducing any material which might be objectionable on the score of inaccurate diagnosis, we have therefore limited this study to patients with syphilitic aortic insufficiency and aortic aneurysm.

The files of the Syphilis Clinic contain the records of 222 patients with aortic regurgitation and 93 with aneurysm. These patients have been followed as carefully as possible by social service visits, search of the in-patient hospital records of the Johns Hopkins Hospital and six other hospitals in Baltimore, and an examination of the death certificates in the Baltimore City Health Department. As a result of this effort, it has so far been possible to trace the ultimate outcome in 90 patients with aortic regurgitation and 43 with aneurysm. The study is still in progress, and these numbers will be augmented in a subsequent communication. To the former group have been added 3 patients with syphilitic aortitis, 3 with syphilitic myocarditis, and 2 with angina pectoris; in all of whom the diagnosis is sufficiently clear cut to be above criticism. A total of 141 patients is thus available for discussion.

TREATMENT METHODS

So far as antisyphilitic treatment is concerned, we have ourselves undergone several changes of attitude. Ten or fifteen years ago, in the relatively early days of arsphenamine, this drug was given to ambulatory patients with cardiovascular syphilis with as much freedom as to other patients with less serious late syphilis. The result of this was a series of four or five immediate deaths on the treatment table, a few instances of sudden death within twenty-four or forty-eight hours (Herxheimer reaction), and a few instances of the sudden precipitation of congestive failure in patients whose compensation had been adequate prior to treatment. Unfortunately the records of many of these older patients have now been lost, so that accurate figures as to the incidence of these untoward accidents cannot be given. Since it was obvious that arsphenamine in average therapeutic dosage could not be given to ambulatory patients without grave risk, this form of treatment was discontinued, and for a period of two or three years our original therapeutic optimism was replaced by an even deeper pessimism. During this period (roughly 1921 to 1923) no treatment except the usual medical measures was employed. Patients seen during these years constitute a large portion of our control untreated material.

With the introduction of bismuth and the gradual recognition of the importance of the therapeutic paradox,* so well emphasized by Wile, the whole question of the treatment of cardiovascular syphilis was reapproached with caution, and with the accumulation of experience our present very elastic system was evolved. The method is not original with us, since other observers, notably Brooks, Schottmüller, Stokes, and Wile have arrived at approximately the same conclusions.

Making all allowances for the fact that the treatment of cardiovascular syphilis is a problem which differs with the individual status of every patient, and which cannot be systematized as can, for example, the treatment of early syphilis, our present scheme is about as follows: if the patient is admitted with congestive heart failure or if he has pronounced pain or frequent attacks of paroxysmal dyspnea without failure, he is placed at rest in bed as promptly as possible. The usual measures are carried out until compensation is regained, when treatment for syphilis is cautiously begun. Both the danger of therapeutic shock (Herxheimer reaction) and that of precipitating decompensation by the too rapid resolution of syphilitic inflammatory tissue (the therapeutic paradox) weigh against the initial use of any of the arsphenamine products. Treatment is started, therefore, with bismuth (or mercury) and potassium iodide. This is continued for at least ten to twelve weeks before any arsenical drug is used, and indeed whether or not an arsenical is ever employed depends largely upon the degree of cardiac reserve which the patient seems capable of accumulating. If this appears adequate, arsenical treatment is started after about three months of preparatory treatment, the drugs of choice being neoarsphenamine or bismarsen (bismuth arsphenamine sulphonate given intramuscularly). The dose of each is small, never exceeding 0.45 gram of neoarsphenamine, usually 0.1 to 0.3 gram at weekly intervals. Courses are long, 10 to 12 injections to a course. Treatment is continuous, courses of neoarsphenamine alternating with courses of bismuth and the iodides, and is kept up for a minimum period of two years, and often indefinitely. It is desirable to avoid treatment reactions of any sort.

RESULTS OF TREATMENT

A study of these 141 patients provides many data of interest and importance, consideration of which must be deferred for a more detailed report. Here we are concerned only with the major question of prolongation of life as a result of treatment. Our results are pre-

*As defined by Wile (The Treatment of the Syphilitic Liver and Heart, A Therapeutic Paradox, Am. J. M. Sc., **164**: 415, 1922), this consists in a remarkable general improvement following arsenical treatment, followed in some cases by a most rapid deterioration with accentuation of the original cardiac defect. Two factors are suggested as explanations: "first that the syphilitic products have been too rapidly replaced by scar tissue, or second, that their rapid disintegration has produced a chemical change deleterious in its effect on the local lesion. . . . We are confronted with the remarkable paradox that the patient gets well or better of his syphilis and may die as the result of the dispersion of his syphilitic cardiac lesion."

sented in tabular form and need little comment. Not a single patient in the whole series had received any antisyphilitic treatment for the cardiovascular lesion before admission, so that the results are based on treatment given under our own observation.

TABLE I

THE EFFECT OF TREATMENT ON THE PROLONGATION OF LIFE IN ANEURYSM OF THE AORTA

TREATMENT	TOTAL CASES	LIVING	DEAD	DURATION OF LIFE UNTIL DEATH OR LAST OBSERVATION, MEASURING FROM	
				ONSET OF SYMPTOMS	START OF TREATMENT
None or very little	11	0	11	9 months	6 months
Equivalent of one course of an arsenical or one long course of a heavy metal (1½-3 months)	12	8	4	34 months	28 months
Equivalent of one long course each of an arsenical and a heavy metal (3-12 months)	8	6	2	28 months	43 months*
More than one year of adequate treatment	12	7	5	69 months	55 months

In this group there were five patients whose aortic aneurysms were discovered in the course of routine physical examination (confirmed in each case by roentgenographic and fluoroscopic examinations), the patients having suffered no symptoms referable to the aneurysm.

In Table I appear the figures as to the ultimate outcome and the duration of life in 43 patients with aortic aneurysm who received varying amounts of treatment. On the basis of the amount of treatment given the patients are divided into four groups: those who got none or very little (one or two injections of an arsphenamine product, or three or four injections of bismuth, or less than a month of mercury by inunction); those who were treated from six to twelve weeks (the equivalent of one arsenical course or one long course of a heavy metal); those treated from three to twelve months (roughly, the equivalent of a long course of an arsenical plus a long course of a heavy metal); and those treated for more than a year. In this and subsequent tables, only those patients are included who (a) are known to be dead or (b) are now in active attendance at the clinic, excepting in this group only one patient who was followed over eleven years but has not been seen for the last eighteen months. It is obvious at once that antisyphilitic treatment does accomplish something in the prolongation of life since, to compare the two extremes, all eleven patients who received no treatment are dead in an average period of nine months from the onset of symptoms; while of those "adequately" treated, 7 of 12 are still alive and the average period from onset of symptoms to death or the present is sixty-nine months.

Such a tabulation is always open to the criticism that the material of the various groups is not strictly comparable, that the lesion in the

untreated group was more serious or more rapidly progressive than in the treated. To judge of the seriousness of cardiovascular syphilis is largely to deal in intangibles, but one can at least summarize the material on the basis of the duration of symptoms and the incidence of congestive cardiac failure prior to the starting of treatment. These data appear in Table II. In the third vertical column is shown the number of patients in whom the aneurysm was discovered at the routine admission physical examination (always confirmed by fluoroscopy), though the patient had as yet suffered no symptoms from its presence. The presence or absence of congestive heart failure, both before and after the start of treatment, is also shown. The fact that in the well treated group symptoms before treatment had existed for an average of eighteen months as compared with an average of six months in each of the other groups, indicates that we have not selected unusually favorable cases for treatment.

We have repeatedly been impressed with the fact that many patients who received only a small amount of treatment failed to return for more because such complete symptomatic relief was obtained that the patient thought he was well.

TABLE II

THE RELATIONSHIP OF THE DURATION OF SYMPTOMS AND OF CARDIAC FAILURE TO THE OUTCOME OF TREATMENT IN ANEURYSM

TREATMENT GROUP	TOTAL CASES	AVERAGE DURATION OF SYMPTOMS BEFORE TREATMENT	PATIENTS SYMPTOMLESS BEFORE TREATMENT	CARDIAC FAILURE	
				BEFORE TREATMENT	AFTER TREATMENT
None or very little	11	6 months	0	6	4 (in 6 cases no data)
Equivalent of one course of an arsenical or one long course of a heavy metal (1½-3 months)	12	6 months	2	3	3 (in 6 cases no data)
Equivalent of one long course each of an arsenical and a heavy metal (3-12 months)	8	6 months	5	0	2 (in 2 cases no data)
More than one year of adequate treatment	12	18 months	1	3	3 (in 1 case no data)

The effect of treatment on the prolongation of life in 98 patients with syphilitic aortic insufficiency (including the 8 miscellaneous patients mentioned above) is shown in Table III.* In this group, the larger number of patients permits a further subdivision on the basis

*Of the 45 living patients in this group, all except 3 are still under observation or treatment. These three were observed for four, six and eight years, respectively.

of the amount of treatment given than in the aneurysm group. Here also the same favorable trend is apparent. For example, of 25 patients not given antisyphilitic treatment, 20 are dead and the average duration of life from the onset of symptoms to death or the present time (if living) is thirty-two months. At the other extreme, of 20 patients receiving more than one year of treatment, all are still living, at an average interval of sixty-five months from the onset of symptoms.

TABLE III

THE EFFECT OF TREATMENT ON THE PROLONGATION OF LIFE IN SYPHILITIC AORTIC INSUFFICIENCY*

TREATMENT	TOTAL CASES	LIVING	DEAD	DURATION OF LIFE UNTIL DEATH OR LAST OBSERVATION, MEASURING FROM	
				ONSET OF SYMPTOMS	START OF TREATMENT
None or very little	25	5	20	32 months	31 months
Equivalent of one short course of an arsenical or one long course of a heavy metal (1½-3 months)	32	7	25	29 months	20 months
Equivalent of two arsenical courses plus a heavy metal (3-6 months)	10	5	5	34 months	31 months
Equivalent of 3 arsenical courses (6-12 months)	11	8	3	54 months	37 months
More than one year of adequate treatment	20	20	—	65 months	58 months

*Including 90 patients with aortic regurgitation, 3 with syphilitic myocarditis, 3 with syphilitic aortitis, and 2 with angina pectoris.

TABLE IV

THE RELATIONSHIP OF THE DURATION OF CARDIAC SYMPTOMS AND OF CARDIAC FAILURE TO THE OUTCOME OF TREATMENT IN AORTIC INSUFFICIENCY

TREATMENT GROUP	TOTAL CASES	AVERAGE DURATION OF SYMPTOMS BEFORE TREATMENT	PATIENTS SYMPTOMLESS BEFORE TREATMENT	CARDIAC FAILURE	
				BEFORE TREATMENT	AFTER TREATMENT
None or very little	25	7 months	1	17	9 (in 16 cases, no data)
Equivalent of one short course of an arsenical or one long course of a heavy metal (1½-3 months)	32	10 months	3	17	17 (in 8 cases, no data)
Equivalent of two arsenical courses plus a heavy metal (3-6 months)	10	3 months	1	4	4 (in 1 case, no data)
Equivalent of 3 arsenical courses (6-12 months)	11	15 months	0	5	7 (in 2 cases, no data)
More than one year of adequate treatment	20	13 months	5	3	1

In these patients it is much more difficult to decide the question of the comparable severity of the lesion in the different treatment groups. An attempt is made in Table IV, on the same basis as in the aneurysm group. Here an outstanding point is that the ultimate outcome is unfavorably influenced by the occurrence of congestive failure before treatment is started, although even a severe degree of failure does not necessarily preclude a favorable outcome. It will be noted that in 5 of 20 patients in the well-treated group, the aortic regurgitation was discovered at the admission physical examination, though as yet the patients had suffered no symptoms from its presence. In the remaining 15, however, symptoms had been present for an average of thirteen months before treatment was started, a period longer than in the least adequately treated groups; and three of the well-treated patients had had pronounced congestive heart failure before treatment.

TABLE V

THE AVERAGE DURATION OF LIFE IN TREATED PATIENTS WITH AORTIC INSUFFIENCY

TREATMENT GROUP	TOTAL CASES	PATIENTS LIVING	AVERAGE DURATION OF LIFE FROM		PATIENTS DEAD	AVERAGE DURATION OF LIFE FROM	
			ONSET OF SYMPTOMS	BEGINNING OF TREATMENT TO PRESENT		ONSET OF SYMPTOMS TO DEATH	BEGINNING OF TREATMENT TO DEATH
None or very little	25	5	52 mo.	------	20	22 mo.	21+ mo.
Equivalent of one short course of an arsenical or one long course of a heavy metal (1½-3 mo.)	32	7	62 mo.	49 mo.	25	21 mo.	12 mo.
Equivalent of two arsenical courses plus a heavy metal (3-6 months)	10	5	48 mo.	45 mo.	5	20 mo.	16 mo.
Equivalent of 3 arsenical courses (6-12 months)	11	8	60 mo.	41 mo.	3	35 mo.	28 mo.
More than one year of adequate treatment	20	20	65 mo.	58 mo.	–	–	–

The question of duration of life in this group is further analyzed in Table V, in which are shown the figures for living and dead patients. The fact that 5 patients who received no treatment whatever are still living after an average period of fifty-two months illustrates the extreme difficulty of evaluating the effect of treatment in an individual patient. Had these 5 patients been treated, one would be tempted to regard them as therapeutic successes. The only fair method of approaching the problem, therefore, is to estimate averages in a large number of fairly comparable cases. When expressed as in this table, the results are less striking than when grouped as in Table III. The intangible

factor incapable of expression in figures is that of the 20 well-treated living patients; many more are partially or completely symptom free and able to do some form of work than those less adequately treated.

SUMMARY AND CONCLUSIONS

1. The treatment of cardiovascular syphilis is best accomplished by a combination of such routine medical measures as rest, restriction of activities, and digitalis together with antisyphilitic treatment.

2. An acceptable method of antisyphilitic treatment is based on the avoidance of therapeutic shock (the Herxheimer reaction) and the therapeutic paradox by starting treatment cautiously with bismuth or mercury and the iodides, by the use of long courses of small doses of neoarsphenamine or bismarsen, and by the prolongation of treatment for a minimum of two years with alternation of these drugs.

3. A study of 43 patients with aortic aneurysm demonstrates that life may be prolonged from an average of nine months from the onset of symptoms in untreated patients, to an average of sixty-nine months in patients receiving one year or more of such treatment.

4. A study of 90 patients with aortic regurgitation and 8 with various other forms of syphilitic cardiovascular disease shows that life may be prolonged from an average of thirty-two months from the onset of symptoms in untreated patients to an average of sixty-five months in patients receiving one year or more of such treatment.

5. These data seem to demonstrate that properly directed antisyphilitic treatment is of great value in cardiovascular syphilis.

DISCUSSION

Dr. Horine, Louisville, Ky.—This brings up an interesting point about which I would like to ask Dr. Danglade. He said the patients did not have aortic insufficiency but had cardiac enlargement. What produced the enlargement?

Dr. Alexander Lambert, New York, N. Y.—In looking back over the experience of thirty-six years at Bellevue Hospital we can feel a degree of satisfaction in that we can give a great deal of benefit to cardiovascular syphilitic cases if we persist in some form of mixed treatment. The trouble is that as soon as patients get better they get careless and drop all forms of treatment and of course they retrograde. The idea that cardiovascular syphilis cannot be treated successfully is erroneous. The old idea was right that cardiovascular syphilis was the one thing that could be treated by mercury. That is the experience of more than one generation.

Dr. Wm. D. Reid, Boston, Mass.—I analyzed the cases at the Massachusetts General Hospital. There were three groups: (1) in which there was only slight treatment, and in this the length of life averaged one year; (2) a group with moderate treatment which averaged three years; and (3) a group with early and prolonged treatment in which many of the patients were able to go back to full physical work, and life was prolonged.

Dr. E. P. Carter, Baltimore, Md.—This study has made very patent the fact that in certain conditions, with proper supervision and proper therapeutic care, we can accomplish a great deal in cardiovascular syphilitics. The question of the subjective relief of symptoms has not been touched upon but the evidence seems to

support a view, which is rather against the impression of some of the men in syphilis clinics, that careful, systematic treatment of cardiovascular syphilis does add to the expectancy of life.

Dr. A. G. Sullivan, Hot Springs National Park, Ark.—It would seem almost impossible to make a diagnosis of syphilitic myocarditis. The myocardium is invaded by the spirochete, but it is extremely difficult to demonstrate clinically the signs and symptoms resulting from that invasion. They are probably due to interference with the coronary blood supply at the coronary openings in the aorta. Therefore, I was interested to know if these cases also had involvement of the aorta.

Dr. E. P. Carter, Baltimore, Md.—I have the impression that there are cases in which one is justified in interpreting the condition as diffuse myocardial disease. I do not believe, however, that all round-celled infiltration is syphilis of the myocardium. We have had 5 cases of individuals between thirty and forty years of age, with marked cardiac failure, watched over a long period, and coming to autopsy with characteristic periarterial focal infiltration regarded by the pathologist as indicating the result of syphilitic change. One case had an acute pericarditis without endocardial disease. There were two cases of early luetic aortitis. The other had true involvement of the aorta. We have no justification for a positive statement that these lesions found histologically are due to the syphilitic virus. It is merely inference. We are not able to find the spirochetes.

Dr. Danglade (closing).—These patients had cardiac enlargement without aortic insufficiency at the original examination. None of them had arterial hypertension. The only explanation I can think of is that the syphilitic process in the myocardium produced weakness with resulting dilatation. One patient came back nine months later much improved by treatment. The cardiac outlines were reduced, and at that time there was a very soft diastolic murmur in the aortic area.

In the three cases mentioned we noted enlarged cardiac outlines (confirmed by x-ray) with widening of the aortic shadow but without aortic insufficiency. Their symptoms were those of myocardial failure, i.e., dyspnea, cyanosis, and dependent edema. There was nothing about the electrocardiogram that was conclusive at all. All had positive serology. We followed them up for from two to fifteen months after leaving the hospital. The diagnosis of syphilitic myocarditis was made after prolonged observation and largely by exclusion. Treatment was started cautiously. The end-results were very striking. Patients came around very slowly, but definite improvement was evident. All three patients mentioned are alive and are maintaining their improved condition.

We have repeatedly been impressed by the fact that patients lapsed from treatment because their symptoms were so promptly relieved. They considered themselves cured, only to return to the clinic anywhere from six to twenty-four months later because of the return of symptoms.

Dr. Moore (closing).—The most important thing in the discussion is really repetition. Dr. Wile made the statement four or five years ago that treatment of cardiovascular syphilis in the prearsphenamine days was satisfactory. Then salvarsan was introduced and used with misguided enthusiasm. I was one who made mistakes. The generation growing up now is impressed with the amount of harm that was done, and some of them have returned to treatment consisting of nothing but rest and digitalis. I think it is clear that if we revise our methods of treatment and include the use of antisyphilitic drugs with more caution, we shall get better results in the treatment of syphilitic cardiovascular disease.

PRINCIPLES UNDERLYING THE TREATMENT OF CARDIOVASCULAR SYPHILIS*

Udo J. Wile, M.D.
Ann Arbor, Mich.

IT IS not only difficult but may be said to be hazardous to lay down axiomatic rules governing the treatment of a syphilitic individual. In no disease of human pathology does the individual enter so largely into the treatment of his case as occurs in syphilis. Age, duration of infection, previous treatment, coincident disease of other nature, social status, weight, and musculature are considerations of greatest importance which must be weighed in every case. However important these desiderata are in treating the patient with early diffuse syphilis, individualization becomes increasingly so when some particular system of the body presents itself as a therapeutic problem due to syphilitic late changes. In discussing the treatment of syphilitic heart disease, therefore, it is possible to lay down only the general principles which might govern the therapeutic procedures and to conform to the excellent general rule that each case in the last analysis presents its individual therapeutic problem.

From the clinico-pathological standpoint, we might first discuss the rare types of syphilitic heart disease which occur early in the course of syphilis. These represent a relatively small, little recognized, and unimportant group. The changes that occur later in the heart and great vessels make up a very large part of the clinical pathology of late syphilitic disease and present the most frequent and most serious of the syphilitic visceropathies. In the late group again we must distinguish those in which syphilitic disease is still active and those cases in which we are dealing with the mechanical end-results of a condition which, while it may progress, does so by degenerative changes rather than by further inroads of the disease itself. In the early group are a few cases of myocardial involvement coincident with or following shortly after the exanthematous period. These are ordinarily ascribed to widespread invasion of the spirochete into the myocardium and consequent early degenerative changes. Occasional sudden death from failure is recorded in this group, and not infrequent attacks of syncope, of heart-block, and of angina-like attacks. In view of the paucity of cases of this kind, and of the meager observations in the literature, it is not possible to lay down adequate criteria for their treatment.

*Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School, service of Dr. Udo J. Wile.

In a very small number of personal observations in which arrhythmia, tachycardia, heart-block, and sudden attacks of syncope have occurred, I have been impressed by the fact that this group responded well to energetic treatment in which the heavy metals have formed the background and in which the arsphenamines have been used sparingly. The relative infrequency of this group makes it seem quite possible that as occurs in other viscera, particularly the liver and kidneys, we may be dealing with subclinical heart involvement due to other causes in which the added insult of spirochetal invasion brings the picture into the foreground.

In the later cases, we must distinguish as particular therapeutic problems the following groups:

1. Energetically treated asymptomatic cases.
2. Energetically treated cases in which cardiovascular dysfunction exists.
3. Inadequately treated asymptomatic cases.
4. Inadequately treated cases with cardiovascular dysfunction.

To these four groups I would add a fifth in which cardiovascular disease, symptomatic or asymptomatic, may exist with other clinically predominant syphilitic visceropathies.

Broadly speaking, Group I represents a type of case in which it is frequently wise even in the presence of serologic evidence to withhold all treatment. Included here, the well compensated cases of aortic regurgitation are by far the most numerous, although included in it are also a few cases of subclinical aortitis and diffuse aortic dilatation.

From a rather wide experience with cases of these types, I have seen many endlessly and futilely treated in the effort to reverse a biological test. The continuous barrage of treatment in patients of this sort who have already had a good or fair background of therapy, in whom adequate compensation for their lesions exists, constitutes in my opinion a class in which more harm than good may be done by energetic antisyphilitic treatment.

In the second group, that is, those energetically treated before the onset of cardiac disease, in which dysfunction exists, I would go further and state that during the stages of decompensation these cases should seldom if ever be treated as syphilis. The therapeutic problem is one of heart failure and the problem is a mechanical defect existing in a degenerated structure. Mercury, bismuth or arsphenamines are of no benefit, and in the presence of edema are definitely contraindicated.

In Group III, cases inadequately treated early, and with asymptomatic cardiovascular disease, much I think may be accomplished by judicious antisyphilitic treatment. To what extent we slow up or

inhibit the progress of such cases or keep them asymptomatic is difficult to determine. No one who ever has seen such cases in large number can fail to be impressed with the fact that many of them remain in a status quo, their physical signs remain, though occasionally even changes for the better are noted, and cardiac dysfunction is definitely postponed for them. Not a small part of their improvement must of course be due to the dispersion of syphilitic residua in other organs of the body, as well as in the bone marrow, spleen, and lymphoid tissues. The presence and persistence of such foci remote from the heart itself must also be recognized as contributory factors in the ultimate cardiac failure in untreated cases.

In the fourth group, inadequately or untreated cases in which cardiac dysfunction exists, we are faced with a very delicate therapeutic problem. These cases again should, I think, seldom if ever be treated for syphilitic disease during the stage of decompensation. After proper rest, digitalization, and other treatment resulting in the building up of their cardiac reserve, judicious treatment on conservative lines directed to the old syphilis is of unquestionable benefit.

Not only are the active foci in the heart itself, and the great vessels beneficially affected in this way, but the remote syphilitic lesions in other parts of the body with their contributory degenerating effects are dispersed.

Of particular importance, I think, at this point is the emphasis that the arsphenamines are not the drugs of choice. I am satisfied from a large number of observations that more harm than good is accomplished by the energetic antisyphilitic treatment of cases recovering from heart failure in this group. Absorption of syphilitic residua and replacement by fibrosis seem safer when slowly accomplished than when induced by energetic therapy. Iodide of potash and mercury or more lately bismuth in moderate doses have in my hands been happier choices than the arsenicals. This group in fact represents one of the few indications where ingested mercury or mixed treatment may judiciously be used, at least in the beginning.

Up to a few years ago, a series of experiences in which I had seen the use of the arsphenamines result in dysfunction and not infrequently in death led me to advise against them in any case of cardiovascular syphilis. However, with the introduction of tryparsamide into the treatment of neurosyphilis, I was early convinced of its great usefulness in certain cases of cardiovascular syphilis, especially in aortitis and in certain early aneurysmal dilatations. Perhaps from its extraordinary tonic effect, perhaps because of specific effect on the process itself, its judicious use is attended with a remarkable improvement in color, strength, and gain in weight so frequently as to merit a real place in the treatment of selected cases. As in the case of the other

arsenicals, however, it should never be used when decompensation is present or where this has already occurred.

The group of cases in which coronary disease is apparently present or suspected from the clinical picture are variously influenced by antisyphilitic treatment. Some seem markedly benefited, others are not influenced and a third group is made definitely worse. My own experience has impressed me with the analogy of these cases to those of cerebral thrombosis. In this condition, the cases occurring relatively early in the disease, particularly in young persons, seem to be greatly benefited and many are arrested or cured by treatment. The later group and particularly older individuals respond less well.

The same seems to hold true with cases of apparent cardiac disease with associated anginoid pains. In both the cases of coronary disease and where angina pectoris as a syndrome is present, the best results are obtained by mercury, bismuth and iodide rather than by the arsphenamines.

Late cases of aneurysm with marked signs and symptoms have in my hands been disappointing in their response to antisyphilitic treatment. This failure to improve takes on added interest in the presence of response in the same patient to other syphilitic processes. I have on several occasions seen cutaneous gummas and syphilitic hepatitis completely relieved as symptom complexes in patients whose aneurysmal process was in nowise benefited.

SUMMARY

The treatment of the syphilitic heart disease is always a treatment of the individual patient. Such cases as are amenable to antisyphilitic régime respond well if not pushed too hard and if treated before decompensation has occurred or after it has been temporarily relieved. The mechanical end-results of syphilitic disease of cardiovascular nature are in no way influenced by antisyphilitic treatment. In those cases of cardiovascular syphilis in which benefit is achieved, this occurs not only because of dispersion of active processes in the affected part of the cardiovascular system, but in a large measure is due to the dispersion of remote foci elsewhere in the body.

Such foci in untreated cases must act as predisposing and contributory factors in the ultimate breakdown of the cardiovascular system. Fully compensated cases of cardiovascular syphilis which have a good background of early treatment are frequently cases which need not and should not be treated. Except for tryparsamide in certain selected cases of aortitis, better results are achieved by the conservative use of mercury, bismuth and iodide than by the arsphenamines. These comments are not intended as dogmatic, incontrovertible statements of fact, but are based entirely upon personal experience.

CLOSING DISCUSSION OF SYMPOSIUM

Dr. Haven Emerson, New York, N. Y.—One of the hazards of a symposium of this kind is that it forces authors into premature publicity. With rare exceptions the numbers of observations reported upon are so small as to forbid reliable use of the statistical method of presentation of results, as has been attempted here in several instances. In the great majority of the papers the correlations which are claimed are not significant, the probable error is of a high degree, and the conclusions are not statistically justified.

In using the mathematical expression of accumulated facts it is well to remember that comparability, objectivity, and reliability of the observed facts are of prime importance.

The statistical method may indicate the trend of facts toward certain conclusions. The critically controlled experiment is usually needed to give a conclusive answer to any question susceptible of scientific proof. The trend of many of the observations reported here today is indicated, but only by much more rigorous critical analysis can these be accepted as valid in view of the paucity of original data and the lack of controlled experiment.

Dr. Henson, St. Paul, Minn.—I think we would like to carry away with us a definite impression of the value of treatment in cardiovascular syphilis. As we listened to the various speakers, we note that they draw their material from different types of patients—from private practice, from hospitals, and from dispensaries. We are confronted by the fact that prognosis is influenced by the type of treatment and the type of lesion. Dr. Herrmann shows that his patients got treatment only for from ten days to two weeks on an average. Dr. Danglade used mercury from three months up to sixty-five months. My own experience is in between these figures, and is drawn from both clinical and private practice. I use mercury for three months, then after a rest I give arsphenamine, 0.05 to 0.15, never giving more than 0.3 gm. I have 10 patients still alive six to ten years after beginning treatment.

Dr. S. R. Roberts, Atlanta, Ga.—As clinicians, and not statisticians, I think that the impression should go out that we need not be discouraged from drawing conclusions from cases. While statistics do show trends, we need not be too pessimistic. We do not have to wait for thousands of cases before publishing our results. After all, statistics are made up of the sum total of little things.

A preliminary note on "The Treatment of Syphilitic Aortic Regurgitation with Congestive Heart Failure," by Drs. George Herrmann and S. Chaille Jackson of New Orleans, La., was read by Dr. Herrmann. The complete report of this work will be published later.

The following papers were read at the meeting of the American Heart Association in Portland, Ore., July 9, 1929, and were published in full in the October, 1929, issue of the AMERICAN HEART JOURNAL.

SYPHILITIC CORONARY OCCLUSION IN AORTIC INSUFFICIENCY

J. H. CANNON, M.D.
CHARLESTON, S. C.

(Summary.) Two cases of syphilitic aortitis with insufficiency and occlusion of a main branch of a coronary artery are reported. The striking similarity of the cases is commented upon, and statistics from analysis of a small series of cases are utilized.

It would seem, therefore, that in young adults with syphilis and aortic insufficiency who do not exhibit the usual compensatory hypertrophy and whose progress is rapidly toward a fatal outcome, one may reasonably presume the involvement of one or more of the coronary openings in the syphilitic process.

ABNORMAL ELECTROCARDIOGRAMS IN PATIENTS WITH SYPHILITIC AORTITIS

IRVING R. JUSTER, M.D., AND HAROLD E. B. PARDEE, M.D.
NEW YORK, N. Y.

(Summary.) Of 50 patients with syphilitic aortitis who were studied, two-thirds had aortic insufficiency and one-third did not; about one-third had aneurysm; 5 had both aortic insufficiency and aneurysm.

In general the patients with aortic insufficiency were older than those without; shortness of breath was their chief complaint, though pain in the anterior chest was frequent, and almost one-third complained of edema. All but one showed a systolic murmur at the aortic area.

The electrocardiogram showed an abnormal T-wave in 85 per cent of these patients, and in 20 per cent it was of the coronary type. It was abnormal in only 38 per cent of those without the valve lesions and 1 case (7 per cent) showed a wave of the coronary type.

Ten autopsies were obtained on these 50 cases, and from a study of the autopsy material and the electrocardiographic records it appeared that the abnormality of the T-wave is probably due to encroachment upon the lumen of the coronary orifices by the syphilitic disease in the sinuses of Valsalva. The greater frequency of the T-wave changes in the group with aortic insufficiency is due to the fact that in these patients the aortitis involves the region of the valves near which the coronary arteries originate.

Changes in the T-wave of patients with syphilitic aortitis should be viewed as an indication of serious coronary involvement, but not necessarily as an indication of myocardial pathology.

This observation has an extremely important bearing upon our general understanding of the causes of abnormality of the T-wave.